# SCIENCE



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ON THE NOTIONS OF CAUSALITY AND COMPLEMENTARITY

NIELS BOHR

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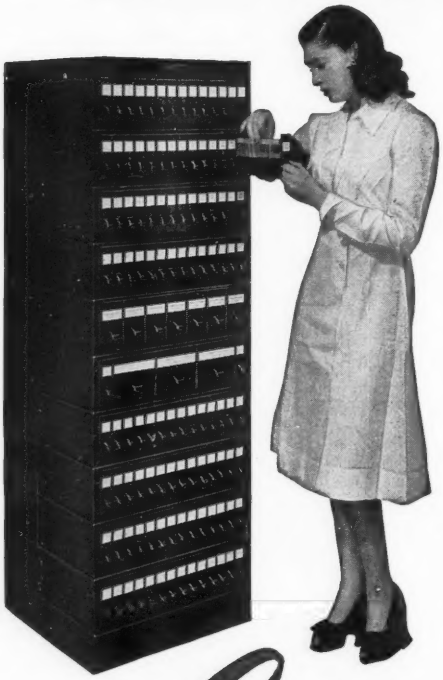

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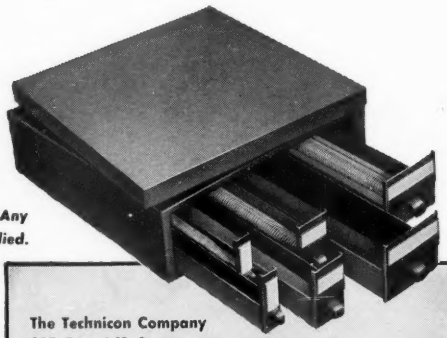

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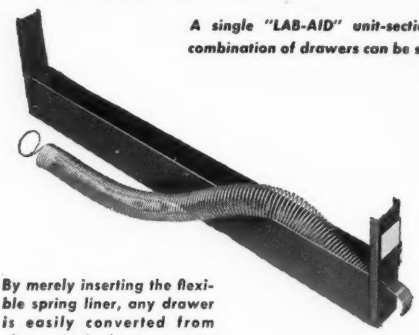

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# On the Notions of Causality and Complementarity[1]

**Niels Bohr**

*Institute for Theoretical Physics, University of Copenhagen, Denmark*

THE CAUSAL MODE of description has deep roots in our conscious endeavors to utilize experience for practical adjustment to our environments, and is in this way inherently incorporated in common language. By the guidance which analysis in terms of cause and effect has offered in many fields of human knowledge, the principle of causality has even come to stand as the ideal for scientific explanation.

In physics, causal description, originally adapted to the problems of mechanics, rests on the assumption that the knowledge of the state of a material system at a given time permits the prediction of its state at any subsequent time. Here, however, already the definition of state requires special consideration and it need hardly be recalled that an adequate analysis of mechanical phenomena was possible only after the recognition that, in the account of a state of a system of bodies, not merely their location at a given moment but also their velocities have to be included.

In classical mechanics, the forces between bodies were assumed to depend simply on the instantaneous positions and velocities; but the discovery of the retardation of electromagnetic effects made it necessary to consider force fields as an essential part of a physical system, and to include in the description of the state of the system at a given time the specification of these fields in every point of space. Yet, as is well known, the establishment of the differential equations connecting the rate of variation of electromagnetic intensities in space and time has made possible a description of electromagnetic phenomena in complete analogy to causal analysis in mechanics.

It is true that, from the point of view of relativistic argumentation, such attributes of physical objects as position and velocity of material bodies, and even electric or magnetic field intensities, can no longer be given an absolute content. Still, relativity theory, which has endued classical physics with unprecedented unity and scope, has just through its elucidation of the conditions for the unambiguous use of elementary physical concepts allowed a concise formulation of the principle of causality along most general lines.

However, a wholly new situation in physical science was created through the discovery of the universal quantum of action, which revealed an elementary feature of "individuality" of atomic processes far beyond the old doctrine of the limited divisibility of matter originally introduced as a foundation for a causal explanation of the specific properties of material substances. This novel feature is not only entirely foreign to the classical theories of mechanics and electromagnetism, but is even irreconcilable with the very idea of causality.

In fact, the specification of the state of a physical system evidently cannot determine the choice between different individual processes of transition to other states, and an account of quantum effects must thus basically operate with the notion of the probabilities of occurrence of the different possible transition processes. We have here to do with a situation essentially different in character from the recourse to statistical methods in the practical dealing with complicated systems that are assumed to obey laws of classical mechanics.

The extent to which ordinary physical pictures fail in accounting for atomic phenomena is strikingly illustrated by the well-known dilemma concerning the corpuscular and wave properties of material particles as well as of electromagnetic radiation. It is further important to realize that any determination of Planck's constant rests upon the comparison between aspects of the phenomena which can be described only by means of pictures not combinable on the basis of classical physical theories. These theories indeed represent merely idealizations of asymptotic validity in the limit where the actions involved in any stage of the analysis of the phenomena are large compared with the elementary quantum.

In this situation, we are faced with the necessity of a radical revision of the foundation for description and explanation of physical phenomena. Here, it

[1] The purpose of this article is to give a very brief survey of some epistemological problems raised in atomic physics. It was originally published in *Dialectica*, International Review of the Philosophy of Knowledge, Editions du Griffon, Neuchâtel, Switzerland, Vol. 7/8 (1948), p. 312. A fuller account of the historical development, illustrated by typical examples which have served to clarify the general principles, is included in a chapter of *Albert Einstein: Philosopher-scientist*, being published by The Library of Living Philosophers, Inc., Evanston, Illinois, under the editorship of Paul Arthur Schilpp.

must above all be recognized that, however far quantum effects transcend the scope of classical physical analysis, the account of the experimental arrangement and the record of the observations must always be expressed in common language supplemented with the terminology of classical physics. This is a simple logical demand, since the word "experiment" can in essence be used only in referring to a situation where we can tell others what we have done and what we have learned.

The very fact that quantum phenomena cannot be analyzed on classical lines thus implies the impossibility of separating a behavior of atomic objects from the interaction of these objects with the measuring instruments which serve to specify the conditions under which the phenomena appear. In particular, the individuality of the typical quantum effects finds proper expression in the circumstance that any attempt at subdividing the phenomena will demand a change in the experimental arrangement, introducing new sources of uncontrollable interaction between objects and measuring instruments.

In this situation, an inherent element of ambiguity is involved in assigning conventional physical attributes to atomic objects. A clear example of such an ambiguity is offered by the dilemma mentioned, as to the properties of electrons or photons, where we are faced with the contrast revealed by the comparison between observations regarding an atomic object, obtained by means of different experimental arrangements. Such empirical evidence exhibits a novel type of relationship, which has no analogue in classical physics and which may conveniently be termed *complementarity* in order to stress that in the contrasting phenomena we have to do with equally essential aspects of all well-defined knowledge about the objects.

An adequate tool for the complementary mode of description is offered by the quantum-mechanical formalism, in which the canonical equations of classical mechanics are retained while the physical variables are replaced by symbolic operators subjected to a noncommutative algebra. In this formalism Planck's constant enters only in the commutation relations

$$qp - pq = \sqrt{-1}\,\frac{h}{2\pi} \qquad (1)$$

between the symbols $q$ and $p$ standing for a pair of conjugate variables, or in the equivalent representation by means of the substitutions of the type

$$p = -\sqrt{-1}\,\frac{h}{2\pi}\frac{\partial}{\partial q} \qquad (2)$$

by which one of each set of conjugate variables is replaced by a differential operator. According to the two alternative procedures, quantum-mechanical calculations may be performed either by representing the variables by matrices with elements referring to the individual transitions between two states of the system or by making use of the so-called wave equation, the solutions of which refer to these states and allow us to derive probabilities for the transitions between them.

The entire formalism is to be considered as a tool for deriving predictions, of definite or statistical character, as regards information obtainable under experimental conditions described in classical terms and specified by means of parameters entering into the algebraic or differential equations of which the matrices or the wave functions, respectively, are solutions. These symbols themselves, as is indicated already by the use of imaginary numbers, are not susceptible to pictorial interpretation; and even derived real functions like densities and currents are only to be regarded as expressing the probabilities for the occurrence of individual events observable under well-defined experimental conditions.

A characteristic feature of the quantum-mechanical description is that the representation of a state of a system can never imply the accurate determination of both members of a pair of conjugate variables $q$ and $p$. In fact, due to the noncommutability of such variables, as expressed by (1) and (2), there will always be a reciprocal relation

$$\Delta q \cdot \Delta p = \frac{h}{4\pi} \qquad (3)$$

between the latitudes $\Delta q$ and $\Delta p$ with which these variables can be fixed. These so-called indeterminacy relations explicitly bear out the limitation of causal analysis, but it is important to recognize that no unambiguous interpretation of such relations can be given in words suited to describe a situation in which physical attributes are objectified in a classical way.

Thus, a sentence like "we cannot know both the momentum and the position of an electron" raises at once questions as to the physical reality of such two attributes, which can be answered only by referring to the mutually exclusive conditions for the unambiguous use of space-time coordination, on the one hand, and dynamical conservation laws, on the other. In fact, any attempt at locating atomic objects in space and time demands an experimental arrangement involving an exchange of momentum and energy, uncontrollable in principle, between the objects and the scales and clocks defining the reference frame. Conversely, no arrangement suitable for the control of momentum and energy balance will admit precise description of the phenomena as a chain of events in space and time.

Strictly speaking, every reference to dynamical concepts implies a classical mechanical analysis of physical evidence which ultimately rests on the recording of space-time coincidences. Thus, also in the descrip-

tion of atomic phenomena, use of momentum and energy variables for the specification of initial conditions and final observations refers implicitly to such analysis and therefore demands that the experimental arrangements used for the purpose have spatial dimensions and operate with time intervals sufficiently large to permit the neglect of the reciprocal indeterminacy expressed by (3). Under these circumstances it is, of course, to a certain degree a matter of convenience to what extent the classical aspects of the phenomena are included in the proper quantum-mechanical treatment where a distinction in principle is made between measuring instruments, the description of which must always be based on space-time pictures, and objects under investigation, about which observable predictions can in general be derived only by the nonvisualizable formalism.

Incidentally, it may be remarked that the construction and the functioning of all apparatus like diaphragms and shutters, serving to define geometry and timing of the experimental arrangements, or photographic plates used for recording the localization of atomic objects, will depend on properties of materials which are themselves essentially determined by the quantum of action. Still, this circumstance is irrelevant for the study of simple atomic phenomena where, in the specification of the experimental conditions, we may to a very high degree of approximation disregard the molecular constitution of the measuring instruments. If only the instruments are sufficiently heavy compared with the atomic objects under investigation, we can in particular neglect the requirements of relation (3) as regards the control of the localization in space and time of the single pieces of apparatus relative to each other.

In representing a generalization of classical mechanics suited to allow for the existence of the quantum of action, quantum mechanics offers a frame sufficiently wide to account for empirical regularities which cannot be comprised in the classical way of description. Besides the characteristic features of atomic stability, which gave the first impetus to the development of quantum mechanics, we may here refer to the peculiar regularities exhibited by systems composed of identical entities, such as photons or electrons, and determining for radiative equilibrium or essential properties of material substances. As is well known, these regularities are adequately described by the symmetry properties of the wave functions representing the state of the whole systems. Of course, such problems cannot be explored by any experimental arrangement suited for the tracing in space and time of each of the identical entities separately.

It is furthermore instructive to consider the conditions for the determination of positional and dynamical variables in a state of a system with several atomic constituents. In fact, although any pair, $q$ and $p$, of conjugate space and momentum variables obeys the rule of noncommutative multiplication expressed by (1), and thus can be fixed only with reciprocal latitudes given by (3), the difference $q_1 - q_2$ between the space coordinates referring to two constituents of a system will commute with the sum $p_1 + p_2$ of the corresponding momentum components, as follows directly from the commutability of $q_1$ with $p_2$ and of $q_2$ with $p_1$. Both $q_1 - q_2$ and $p_1 + p_2$ can, therefore, be accurately fixed in a state of the complex system and we can consequently predict the value of either $q_1$ or $p_1$ if either $q_2$ or $p_2$ respectively, is determined by direct measurement. Since at the moment of measurement the direct interaction between the objects may have ceased, it might thus appear that both $q_1$ and $p_1$ were to be regarded as well-defined physical attributes of the isolated object and that, therefore, as has been argued, the quantum-mechanical representation of a state should not offer an adequate means of a complete description of physical reality. With regard to such an argument, however, it must be stressed that any two arrangements which admit accurate measurements of $q_2$ and $p_2$ will be mutually exclusive and that therefore predictions as regards $q_1$ or $p_1$ respectively, will pertain to phenomena which basically are of complementary character.

As regards the question of the completeness of the quantum-mechanical mode of description, it must be recognized that we are dealing with a mathematically consistent scheme which is adapted within its scope to every process of measurement and the adequacy of which can be judged only from a comparison of the predicted results with actual observations. In this connection, it is essential to note that, in any well-defined application of quantum mechanics, it is necessary to specify the whole experimental arrangement and that, in particular, the possibility of disposing of the parameters defining the quantum-mechanical problem just corresponds to our freedom of constructing and handling the measuring apparatus, which in turn means the freedom to choose between the different complementary types of phenomena we wish to study.

In order to avoid logical inconsistencies in the account of this unfamiliar situation, great care in all questions of terminology and dialectics is obviously imperative. Thus, phrases often found in the physical literature, like "disturbance of phenomena by observation" or "creation of physical attributes of objects by measurements," represent a use of words like *phenomena* and *observation* as well as *attribute* and *measurement* which is hardly compatible with common usage and practical definition and, therefore, is apt to cause confusion. As a more appropriate way

of expression, one may strongly advocate limitation of the use of the word *phenomenon* to refer exclusively to observations obtained under specified circumstances, including an account of the whole experiment.

With this terminology, the observational problem in atomic physics is free of any special intricacy, since in actual experiments all evidence pertains to observations obtained under reproducible conditions and is expressed by unambiguous statements referring to the registration of the point at which an atomic particle arrives on a photographic plate or to a corresponding record of some other amplification device. Moreover, the circumstance that all such observations involve processes of essentially irreversible character lends to each phenomenon just that inherent feature of completion which is demanded for its well-defined interpretation within the framework of quantum mechanics.

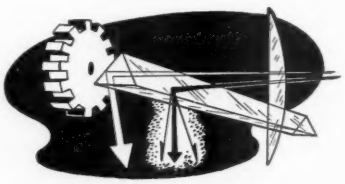
Recapitulating, the impossibility of subdividing the individual quantum effects and of separating a behavior of the objects from their interaction with the measuring instruments serving to define the conditions under which the phenomena appear implies an ambiguity in assigning conventional attributes to atomic objects which calls for a reconsideration of our attitude towards the problem of physical explanation. In this novel situation, even the old question of an ultimate determinacy of natural phenomena has lost its conceptional basis, and it is against this background that the viewpoint of complementarity presents itself as a rational generalization of the very ideal of causality.

The complementary mode of description does indeed not involve any arbitrary renunciation of customary demands of explanation but, on the contrary, aims at an appropriate dialectic expression for the actual conditions of analysis and synthesis in atomic physics. Incidentally, it would seem that the recourse to three-valued logic, sometimes proposed as means for dealing with the paradoxical features of quantum theory, is not suited to give a clearer account of the situation, since all well-defined experimental evidence, even if it cannot be analyzed in terms of classical physics, must be expressed in ordinary language making use of common logic.

The epistemological lesson we have received from the new development in physical science, where the problems enable a comparatively concise formulation of principles, may also suggest lines of approach in other domains of knowledge where the situation is of essentially less accessible character. An example is offered in biology, where mechanistic and vitalistic arguments are used in a typically complementary manner. In sociology, too, such dialectics may often be useful, particularly in problems confronting us in the study and comparison of human cultures, where we have to cope with the element of complacency inherent in every national culture and manifesting itself in prejudices which obviously cannot be appreciated from the standpoint of other nations.

Recognition of complementary relationship is not least required in psychology, where the conditions for analysis and synthesis of experience exhibit striking analogy with the situation in atomic physics. In fact, the use of words like *thoughts* and *sentiments,* equally indispensable to illustrate the diversity of psychical experience, pertain to mutually exclusive situations characterized by a different drawing of the line of separation between subject and object. In particular, the place left for the feeling of volition is afforded by the very circumstance that situations where we experience freedom of will are incompatible with psychological situations where causal analysis is reasonably attempted. In other words, when we use the phrase "I will" we renounce explanatory argumentation.

Altogether, the approach towards the problem of explanation that is embodied in the notion of complementarity suggests itself in our position as conscious beings and recalls forcefully the teaching of ancient thinkers that, in the search for a harmonious attitude towards life, it must never be forgotten that we ourselves are both actors and spectators in the drama of existence. To such an utterance applies, of course, as well as to most of the sentences in this article from the beginning to the end, the recognition that our task can only be to aim at communicating experiences and views to others by means of language, in which the practical use of every word stands in a complementary relation to attempts of its strict definition.



# *In Memoriam*

## Leonor Michaelis: 1875–1949

SCIENCE lost a remarkable character in the death of Leonor Michaelis on October 8, 1949. In the early years of his academic career he contributed to embryology and histology and in the closing years he was applying magnetochemistry to his studies of semiquinones. In the interval he pioneered in the application of the theory of acid-base equilibria to biological problems, he propounded that theory of the competitive action of inhibitors which governs a large sector of this field of enzymology, he contributed invaluable data on semipermeable membranes, and he developed by means of numerous specific cases his theory of single electron exchange in oxidation-reduction systems.

These are but a few of the many topics which might be cited to show the range of his interests. But no citation of a mere bibliography would suffice to convey the flavor of his writing. Dr. Michaelis seems to have had a passion for seeking the broad generalization, yet this was always tempered by the realization that each investigation must be so restricted as to be amenable to quantitative study and so can cover but a small sector of the field. Thus the readers of each of his many papers must have said to themselves: Here is something that is good in itself and has broad implications.

Born in Berlin, Michaelis became cosmopolitan in science, art and the world. An embryologist under Hertwig, a histologist under Paul Ehrlich, a bacteriologist in Rona's laboratory, Michaelis himself inclined toward the application of physicochemical principles to biological and biochemical problems. So it was that as the years passed he became an author of texts on applied mathematics, hydrogen ions, and oxidation-reduction, and of articles on potentiometry and magnetochemistry. Withal, he found time to indulge his love of music and characteristically he carried on to original composition and to the entertainment of his friends with charming improvisations on the piano. The year 1922 found him in Japan studying semipermeable membranes and the effects of electrolytes on colloids. Four years later he displayed his broad knowledge in consulting with members of the Department of Medicine at Hopkins. Thence he went to the Rockefeller Institute for Medical Research, where he became a member. It was there that Michaelis developed his theory of semiquinones and isolated and characterized ferritin. He became an American citizen and a member of the National Academy of Sciences.

After age had forced his formal retirement, Dr. Michaelis remained the enthusiastic investigator and displayed his eagerness to be helpful. At a conference there arose for the moment a question regarding bond energies which he undertook to explain. When the questioners swung to the more elementary matters Dr. Michaelis offered to organize a class on the application of quantum mechanics to valence problems.

There is a passage in a translation of *The book of the courtier* by the Rennaissance author, Castiglione, that reads: "That therefore which is the principall matter and necessarie for a Courtier to speake and write well I believe is knowledge. For he that hath not knowledge and the thing in his mind that deserveth to bee understood can neither speake nor write well." Leonor Michaelis always knew of what he spoke and this shows and shines in his writings. We in America did not know him as a teacher in a teaching post. But whether in casual conversation, in a conference where he was at the fore in preserving perspective, or in his books, we knew him as a great teacher. He had the thing in mind that deserveth to be understood and frequently it was a subject new at the time to biologist or biochemist and that should be understood as prerequisite to the next advance.

As one whose work occasionally overlapped that of Dr. Michaelis, I wish to say that he taught me much and that true to the instincts of a good teacher he generously ignored the fact that I had had an opportunity to find what he later discovered. I am sure I speak for a host of friends in saying that we shall miss his sprightly manner and keen remarks at meetings and that for a long time to come we shall be studying several of his scientific papers.

W. MANSFIELD CLARK
*The Johns Hopkins School of Medicine*
*Baltimore, Maryland*

## Alfred Lee Franklin: 1919–1949

ALFRED FRANKLIN, biochemist, died of nephritis in the Cedars of Lebanon Hospital, Los Angeles, on March 25 at the age of 29. He was born in Los Angeles and was graduated from the University of California, where he received the degrees of A.B. in 1942 and Ph.D. in 1946.

During his short but brilliant scientific career he published several important findings. He reported the effect of goitrogens on the utilization of iodine by the thyroid gland. He observed that an antagonist of folic acid would reduce the white blood cell count of rats to extremely low levels. This observation was made the basis of a proposal that folic acid antagonists

should be used to control certain blood dyscrasias. He studied the metabolism of folic acid and its conjugates, the effects of thiouracil when used in fattening pigs and chickens, and the amino acid composition of the pituitary growth hormone. He collaborated in investigations of the animal protein factor and in the assay of the antipernicious anemia factor. He was a member of the Society for Experimental Biology and Medicine and the American Chemical Society. His personality was vigorous, forthright, and engaging, and his life showed great promise.

THOMAS H. JUKES

*Lederle Laboratories Division*
*American Cyanamid Company,*
*Pearl River, New York*

## Ralph R. Parker: 1888–1949

THE LIFE of Ralph Robinson Parker was closely associated with the long history of the study of Rocky Mountain spotted fever and the development of the Rocky Mountain Laboratory, a story which in some respects is unique in medical history.

Parker, born in Malden, Massachusetts, was educated in entomology at the Massachusetts Agricultural College (now the University of Massachusetts). His father was a physician and was at one time in charge of a leprosarium maintained by the city of Boston. While a graduate student, Parker conducted a study on the possible relationship of flies to transmission of leprosy, which was the subject of his first recorded publication, in May 1914.

While working for his doctorate in 1914, Parker was invited to come to Montana by Robert E. Cooley, who had been state entomologist since 1903, and who was one of the pioneer figures in the study of Rocky Mountain spotted fever. Among Cooley's many responsibilities was investigating the possible relationship of flies to typhoid fever, which was widespread in Montana, and young Parker spent the summer of 1914 studying flies in the Yellowstone Valley. In 1915 Rocky Mountain spotted fever was recognized for the first time in eastern Montana, and Cooley assigned Parker to make preliminary studies on tick infestation on the Powder River. The next year, having received his Ph.D., Parker returned to Montana, this time permanently, with his bride. They lived in a log cabin on the Powder River, and Mrs. Parker spent the spring and summer assisting her husband in collecting ticks from a wide variety of animals which he shot and trapped.

After a year studying ticks on the Musselshell River, Parker was assigned to the spotted fever work in the Bitter Root Valley and in 1918 set up his laboratory in a woodshed at the town of Victor. By that time, the natural history of Rocky Mountain spotted fever had come to be fairly well understood. Known in the Bitter Root Valley since 1873, the disease was greatly feared because of its high mortality. Earle Strain, of Great Falls, had suggested in 1902 that ticks might be the vector of spotted fever, which up to that time was believed to be caused by the drinking of melted snow water. L. B. Wilson and W. M. Chowning, of the University of Minnesota, had gone to the Bitter Root Valley in 1902 at the suggestion of A. F. Longeway, the Montana state health officer, and after several years of study they became convinced that ticks were responsible for the transmission of the disease, but it remained for H. T. Ricketts, of the University of Chicago, to make the actual demonstration in 1906. (Drs. McCalla and Brereton in Idaho had earlier allowed a tick from a spotted fever patient to bite a volunteer, who subsequently developed the disease, but their experiment was not published.)

At the time of Dr. Parker's move to Victor, the problem of Rocky Mountain spotted fever had become largely one of how to develop existing knowledge in order to bring about a reduction in the extent of infection. Parker devoted his efforts to extending the areas of control, systematizing methods of decreasing the tick population, and learning more about the factors influencing the propagation of the infection in ticks. Methods of control then in use did not prove satisfactory, and the death from spotted fever of a prominent Missoula citizen and his wife in 1921 led to an appeal to the U. S. Public Health Service to reenter the spotted fever studies, from which it had withdrawn in 1917 after an active part in the earlier investigations in the Bitter Root. As a result of this appeal, Thomas Parran, who was later to become surgeon general of the Public Health Service, was sent by the then surgeon general, Hugh S. Cumming, to the Bitter Root in 1921. Parran recommended that the Public Health Service renew the studies on spotted fever, and as a result Parker was appointed as a special expert, and a new laboratory was established in an abandoned school building west of Hamilton. This marked the actual birth of the Rocky Mountain Laboratory, as it is known today. Parker was designated as officer in temporary charge at the time of the opening of the laboratory in 1921, and from then on, until the time of his death 28 years later, he was either in actual charge of operations of the laboratory or taking a leading part in them.

In 1922, R. R. Spencer, of the Public Health Service, was assigned to take charge of the Rocky Mountain Laboratory, and for six years he and Parker collaborated in a wide variety of studies on spotted fever and other diseases. This collaboration is most

noteworthy, because it resulted in the development of a vaccine, prepared from infected ticks, which was capable of immunizing human beings against Rocky Mountain spotted fever. Spencer prepared the first vaccine during the winter of 1923–24 while he was at the Hygienic Laboratory in Washington, and was himself the first person to be inoculated. Subsequently, he and Parker were able to demonstrate its effectiveness in experimental animals and in humans.

Construction of a new laboratory at Hamilton was begun in 1927. This building was constructed chiefly for the preparation of tick vaccine and continuation of studies on spotted fever. The Public Health Service purchased the building in 1930, and with subsequent additions it constitutes the present Rocky Mountain Laboratory.

While Parker's initial interest in the Bitter Root was the relationship of ticks to spotted fever, his scientific curiosity was tremendous, and during the course of an unusually productive career he turned his attention to a wide variety of diseases to which he was wont to refer as "diseases of nature," by which he meant diseases of indigenous animals communicable to man, usually via arthropods. In 1923, Parker, Spencer, and Edward Francis published the first report of tularemia in ticks, indicating that this infection could be contracted from sources other than direct contacts with rabbits or bites of deer flies. From then on, tularemia was one of Parker's major interests, and he was actively concerned in investigations, not only on its transmission by ticks and on differing manifestations in various species of mammalian hosts, but also upon the widespread contamination of natural streams of water in the West with the organism *Pasteurella tularensis*, first reported by him and his colleagues in 1940. Ever eager to turn his attention to new fields, he became interested in the study of Q fever after the causative organism had been recovered from ticks by the staff of the Rocky Mountain Laboratory in 1939, and he participated in the recent extensive studies on this subject, which are still in progress. Among what he called diseases of nature is plague, which was recognized in Montana in 1935, for the first time, as a result of work by the staff of the Rocky Mountain Laboratory. With his colleagues, he described the rickettsial disease of the tick *Amblyomma maculatum* in 1939, and was engaged up to the time of his death in studying the relationship between this disease and spotted fever.

As the manufacture of Rocky Mountain spotted fever vaccine became a major operation at the Hamilton laboratory, which was the only source of such material for many years, Parker was impressed with the fact that the procedure was cumbersome and expensive and should be improved. He was instrumental in getting Herald R. Cox to join the staff of the laboratory in order to investigate this problem, with the result that Cox developed the chick embryo type of vaccine which is now the standard method of immunization against spotted fever.

When the Public Health Service was faced with the necessity of providing yellow fever vaccine shortly before the beginning of World War II, Parker, with characteristic energy, made the facilities of the Rocky Mountain Laboratory available, and the vaccine was produced there all through the war under the direct supervision of Mason V. Hargett, who joined the staff for that purpose. This still remains the only source of yellow fever vaccine in North America.

Parker implemented his boundless scientific curiosity with a tremendous industry and a most unusual capacity for work. From 1914 to 1949, he was the author or joint author of 148 scientific papers on entomology and the diseases of nature. The Rocky Mountain Laboratory, with which almost his entire adult life was so intimately bound up, and which must be considered a monument to his ability and industry, is now known throughout the world wherever biological science is known. Probably nowhere today do better facilities exist for complete and thorough studies of the diseases of nature, and the staff Parker attracted to Hamilton comprises specialists, particularly in entomology, who are respected throughout the world as authorities in their fields. As knowledge increased relative to the natural history of the diseases in which Parker and his staff were interested, he added men trained in biochemistry, immunology, bacterial physiology, and virology to complement the renowned group of entomologists and bacteriologists who have been at Hamilton for many years.

Dr. Parker died suddenly on September 4, without previous illness and while at the very peak of scientific and administrative activity. He was enthusiastically concerned with scientific investigations and with further development of the Hamilton laboratory to the time of his death.

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# Technical Papers

## Carbon 14 Beta Track Autoradiography[1, 2]

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Autoradiographs produced by beta particles from histological specimens have until now consisted of randomly distributed silver grains. As a beta particle passes through an emulsion of low sensitivity, only a small number of grains are made developable. The random distribution of these grains (in some cases only one grain per beta particle is produced) does not give a characteristic signature of the path sufficient to identify a single disintegrating atom.

Such a signature, or track, of alpha particles has been used to detect alpha-emitting atoms in tissues (4). When the tissue is placed directly on the emulsion, location of a distintegrated atom can be approximated in the cell by changing the focal plane of the microscope, thereby following the track to its origin at the surface of the emulsion just beneath the cell.

Alpha particles, whose energies and ionizing potentials are much higher than those of beta particles, give well-defined, straight tracks of developed silver grains in nuclear track emulsions. Until recently none of the nuclear track emulsions would show beta tracks. Photographic manufacturers in England and in this country have now developed emulsions which show tracks of beta particles approaching an energy of one Mev. These emulsions have been so sensitive that long exposures of histological specimens having a low concentration of, for example, $C^{14}$, lead to unsatisfactory results. This is owing to an accumulation of a large background of tracks from cosmic events. The Eastman Kodak Research Laboratory recently made an emulsion of intermediate sensitivity with which we have registered $C^{14}$ beta tracks beneath a tissue section in considerable excess of the background tracks. These emulsions also enable one to follow the track of the beta particle to its point of entry.

Two experimental NTB emulsions on glass plates, No. 416,297, 100μ and No. 417,104, 25μ thick, were prepared to have a sensitivity such that they would register as tracks only beta particles up to approximately 0.4 Mev.

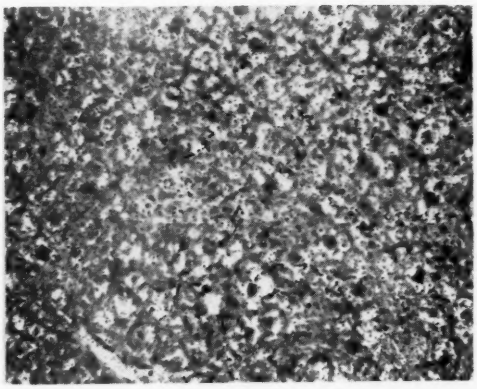

FIG. 1. Photomicrograph of an autoradiograph of a liver section from a rat injected with $C^{14}$-labeled glycine. Magnification × 360. The plane of focus of the microscope is immediately beneath the section, making the cells appear unsharp while a number of beta tracks are sharp.

These emulsions are now designated as NTB2. It is this feature that makes possible the registration of $C^{14}$ beta particles with a maximum energy of 0.165 Mev without registering much random ionization.

The liver section of a rat injected with glycine labeled with $C^{14}$ in its alpha carbon atom was studied. (Autoradiographs of blood cells from this same rat were previously reported (*2*). Three μc was given intraperitoneally and the rat was sacrificed after 25 hr. The tissue was fixed in Bouin's solution, embedded in paraffin, and cut at approximately 7μ. A tissue section was floated on water and picked up by slipping the photographic plate beneath it in the water and lifting the tissue out on the emulsion (*4, 5*). After partial drying, the plate was placed in a black plastic slide-box and set aside in a cold room at approximately 7° C for exposure. Several grams of a desiccant ($CaCl_2$) was placed in the box to keep the humidity low, in order to delay decay of latent images. After exposure and removal of the paraffin (*4, 5*), the plates were developed in Eastman D19 for 20 min and fixed in 30% hypo at approximately 20° C. The tissue was stained in hematoxylin and eosin and mounted in the conventional manner.

The emulsion underneath the tissue sections showed about the same number of random grains as parts of the emulsion outside the area of the sections. However, we have found a large number of beta tracks, the majority of them starting very close underneath the tissue and ending further down in the emulsion (cf. Fig. 1). It is typical of these beta tracks, in contrast to straight alpha tracks, that they are curved, frequently showing sharp bends in any direction. The grain density increases markedly as the particles lose energy by collisions, and the tracks often end in a hook or loop of high grain density. Although most of the tracks we have observed

[1] Based in part on work performed under contract with the U. S. Atomic Energy Commission at the University Atomic Energy Project, Rochester, New York.

[2] The authors wish to thank Dr. John Spence of Eastman Kodak Research Laboratories for preparation of the nuclear track plates, Dr. Kurt Heinicke of the Heinicke Instrument Corporation, Rochester, for the loan of the fluorite objective, and Mr. Robert Hay for making the composite picture of Fig. 2.

[3] Working on a fellowship from the Rask Orsted Foundation, Copenhagen.

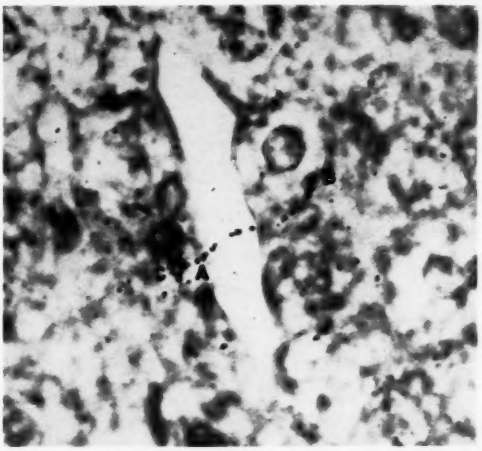

FIG. 2. Photomicrograph of an autoradiograph of a liver section from a rat injected with $C^{14}$-labeled glycine. Magnification × 900. A composite photomicrograph of a view at tissue level and a mosaic of a beta particle track in the emulsion. The photomicrograph of the tissue was taken at a focal plane just above the tissue-emulsion interface. The composite of the track, starting at the interface and running in three dimensions in the emulsion, was made in the manner presently used for the study of the physics of nuclear tracks. These were superimposed and rephotographed. The increasing grain density along the track shows that the beta particle entered the emulsion near *A* and stopped (at a lower point in the emulsion) at *B*. The clump of grains at *C* may indicate a lower energy beta particle which suffered several deflections, but of this we cannot be certain. The cell nucleus near the origin of the track has been slightly retouched to show its size relative to the silver grains.

started in the proximity of the tissue section, not all of them can actually be retraced to a well-defined locus or a part of a cell. A detailed statistical analysis of tracks is required in order to decide such questions as the cytological location and histological distribution of the $C^{14}$. We have also observed tracks starting almost in the middle of the emulsion and running in all directions. Such tracks may be due to random cosmic events, to radioactive substances naturally occurring in the tissue and gelatin, and to photoelectrons from x-rays generated by the beta particle.

Fig. 1 is a photomicrograph of beta particle tracks immediately beneath a liver section. This was taken with a 4.3-mm fluorite objective having a depth of focus of several microns in the central portion of the field. Thus a higher proportion of the three-dimensional tracks can be seen. The objective was focused just beneath the tissue-emulsion interface, giving sharply focused tracks in the center and recognizable cell nuclei in the fringing field for comparison.

To prove that the tracks were made by beta particles from the injected $C^{14}$, and not by background ionizing particles, counts of the number of tracks per field under the tissues were compared with the background of the emulsion which did not support a tissue section. The tracks were countered under oil immersion and while focusing up and down through the emulsion. The following results show that the tracks were produced by $C^{14}$ beta particles:

| | Tracks per field |
|---|---|
| Mean of 40 fields beneath tissue | 18 |
| Mean of 20 fields of emulsion unassociated with tissue (background) | 2 |
| Corrected mean | 16 |
| $\sigma$, Standard deviation | 5.5 |

The $C^{14}$ activity of the liver was determined by means of an ionization chamber, as described elsewhere (*1*). On the basis of these measurements, we have calculated that the quantity of tissue delineated by one field (a field volume of $75 \times 75 \times 7$ $\mu^3$) in the microscope can be estimated to have an activity of approximately 20 disintegrations per day, assuming uniform distribution. The autoradiograph exposure time was ten days, which would give approximately 200 disintegrations in the field volume. However, this figure requires several corrections. We have to take into account: 1) a reduction of about 60% for self-absorption of soft beta rays in the tissue section of 7 $\mu$ thickness (*6*); 2) a reduction slightly greater than 50% for geometry; 3) an unknown factor for latent image fading; and 4) an unknown amount for failure to count low energy beta particles because of our criterion in defining a track.

A minimum track was defined as four closely spaced grains. Hence, beta particles with an energy insufficient to produce a track of at least four grains would not be counted. Also, it is probable that one or two grains in a row can be lost due to latent image fading. In that case, tracks consisting of 4 or 5 grains would no longer pass the criterion of a track. Since a track of three grains represents a beta particle energy of approximately 20–25 kev, all particles of this energy value and below would not be counted.

Applying the first two corrections, approximately 40 beta particles enter the emulsion. The number of countable tracks is less and by applying Corrections 3 and 4 the value of 16 tracks per field is approached. Thus, we arrived at a reasonable agreement between the results of track counting and ionization chamber measurements for this first attempt at quantitative autoradiography.

We have recently shown that autoradiography of isolated cells offers information about the uptake of a metabolite (*3*). For example, random grain autographs of yeast cells indicate a nonuniform uptake of $P^{32}$. The technique of counting individual tracks as described above suggests the possibility of a similar study in a histological specimen. In view of this new possibility, we plan to determine the track density under the peripheral and central cells of the liver lobules to investigate the nonuniformity of distribution of labeled compounds.

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## A Technique for Sectioning Microfossils

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In recent years the sectioning of microfossils (Bryozoa and Foraminifera, especially fusulinids) has been a technique useful to the taxonomist, as well as the general worker in the field of invertebrate micropaleontology. Following the war, several plastics have appeared on the market to compete with Canada Balsam as a mounting medium in sectioning. After experimenting with a number of these plastics, the writer has found that a thermoplastic manufactured by The Lakeside Chemical Corporation[1] gives excellent results with calcareous forms. This type of thermoplastic has a distinct advantage over other media in that it has the same resistance to the grinding agent as does the calcite of the fossil, thus leaving a smooth, unpitted surface.

The present sectioning technique was developed while the writer was studying the shell structure of fossil Ostracoda (a report is now in manuscript). Because of their minute size, average 0.8 mm–1.5 mm, sectioning these bivalved crustaceans has been difficult and time-consuming; in most instances, however, only 15 min is needed to obtain excellent sections with the technique outlined here.

A slide is prepared by heating a very small quantity of the thermoplastic just above the temperature at which it becomes fluid. As quickly as possible the slide is placed on a piece of asbestos under a binocular microscope (magnification 30×) and a double-valved specimen (of an ostracode) is introduced into the plastic. The thermoplastic usually remains fluid for a sufficient time for the specimen to be oriented in any desired position. A fine needle is a satisfactory tool for changing the position of the specimen, the dorsal margin of which may be painted red to aid in orientation. This is accomplished by applying pigment from a colored pencil with a fine brush. The slide is ground by hand in a water mixture of 400-mesh carborundum on a glass plate. The specimen can be examined periodically from the reverse side of the slide, and just before the section is ground to include the desired features the slide is buffed lightly on a power-wheel felt buffer, using a liquid rouge. Suction cups (from toy arrows) with the same diameter as the slide afford an easy method for holding the slide against the buffer. The specimen then is washed thoroughly to remove the rouge and dried. In some instances, if the specimen is first moistened, the results of this part of the process offer sufficient detail to photograph well, using reflected light, although more intricate detail is usually shown if a thin section is made. If a thin section is desired the slide is reheated gently to the melting point of the plastic and the specimen oriented under the microscope so that its flat surface is flush against the slide. It is reground and buffed, as before, until clear structures are obtained.

It is possible to section both single and double valves of fossil ostracodes by this method, but double valves are preferred, since they are easier to orient. Excellent sections of single and double valves of micropelecypods and microbrachiopods were also made by this process.

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## The Fate of Plasma Cells

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Plasma cells are generally believed to be specifically differentiated elements which are apparently unable to change into another cell type and finally degenerate. Only a few authors (*1*, *2*) have admitted the possibility of the transformation of these elements into connective tissue cells.

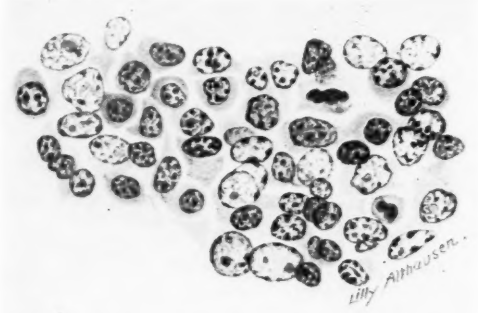


FIG. 1. Medulla of a lymph node: a group of cells is shown in which several intermediate phases from plasma cells to reticular elements are seen; upper right, a mitosis. Magnification × 900.

Recent observations which I made in the course of a study on the histopathology of experimental C-avitaminosis in guinea pigs support the theory of transformation. In fact, histological examination of the lymph nodes, especially from animals submitted to a prolonged hypovitaminotic diet, revealed very clearly that plasma cells undergo a transformation into reticular elements. The plasma cells, initially accumulated in great numbers in the medulla of the lymph nodes, showed a series of transitional phases with numerous mitoses before assuming the aspect of reticular cells. In animals which were kept in hypovitaminosis for longer periods, the plasma cellular infiltrate was sometimes replaced by dense reticular tissue. Similar observations were made in chronic inflammatory tissues from man and animals.

The findings here described confirm the assumption that plasma cells are not doomed to degeneration and suggest that they are cells in a phase of resistance, still maintaining an evident capacity for proliferation and differentiation.

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## Isolation of 17-Hydroxy 11-Dehydro Corticosterone (Kendall's Compound E) from Urine of Normal Males

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In the course of attempting to recover adrenocortical compounds from urine it has been possible to isolate 17-hydroxy 11-dehydro corticosterone from a chloroform extract of pooled normal male urine obtained prior to hydrolysis.

Urine was collected daily and extracted with chloroform without prior adjustment of pH. The extracts were concentrated to a small volume *in vacuo* and stored in the cold. At weekly intervals the pooled extracts were washed with cold 0.1 *N* NaOH and water, taken to dryness *in vacuo*, and stored under nitrogen in the cold. Ultimately the dried residues from 1000 l of urine were combined and part of the caffeine was removed by crystallization from benzene. The nonerystalline portion was divided into 70% alcohol-soluble and petroleum ether-soluble components, and after reduction to dryness *in vacuo* the alcohol-soluble fraction was dissolved in benzene and repeatedly extracted with equal volumes of water. The ketonic parts of both the benzene-soluble and water-soluble fractions were recovered and in turn repeatedly partitioned between benzene and water, using the method outlined by Mason, Myers, and Kendall (*2*). The fraction which passed readily from benzene to water and from water to benzene (designated fraction III by Mason *et al.*) weighed 161 mg and upon being reduced to dryness from chloroform solution crystallized spontaneously.

The first and subsequent crops were recrystallized from absolute ethanol to give 32 mg of colorless rhombohedra, mp 215–218° C. On admixture with an authentic sample of 17-hydroxy 11-dehydro corticosterone (mp 216–218° C) the mp was 215–218° C. Analysis: Calculated for $C_{21}H_{28}O_5$—C = 69.96%, H = 7.83%. Found—C = 69.50, 69.80%, H = 7.61, 7.70%. The addition of concentrated sulfuric acid to a small amount of the crystalline compound gave a yellow solution with a faint green fluorescence. Methanolic solutions of the substance rapidly reduced ammoniacal silver in the cold and formed a bright red precipitate upon the addition of a few drops of a saturated solution of 2,4 dinitrophenylhydrazine in 2 *N* HCl. $[\alpha]_D^{28} = +214° \pm 2°$ (concentration, 0.604 in 95% ethanol). Mason, Myers, and Kendall (*3*) have recorded from 17-hydroxy 11-dehydro corticosterone $[\alpha]_{5461}^{25} = +248° \pm 4°$ (concentration, 0.1 to 0.2), Kuizenga and Cartland (*1*) $[\alpha]_D^{25} = +195°$ (concentration, 1.89), and Wintersteiner and Pfiffner (*4*) $[\alpha]_D^{25} = +209° \pm 1°$ (concentration = 1.2) (all in 95% ethanol).

The compound readily formed an acetate on treatment with a mixture of pyridine and acetic anhydride at room temperature. Recrystallization from absolute ethanol yielded fine needles, mp 236–239° C. On admixture with an authentic preparation of 17-hydroxy 11-dehydro corticosterone acetate (mp 237°–239° C), the mp was 236°–239° C. Analysis of the acetate: Calculated for $C_{23}H_{30}O_6$—C = 68.65%, H = 7.46%. Found—C = 68.41%, H = 7.14%. The compound showed an absorption maximum in the ultraviolet at 237–238 mμ. ε = 13,870 (absolute ethanol). Mason, Myers, and Kendall (*2*) observed an absorption maximum at 237 mμ and have recorded a molecular extinction coefficient of 16,150. The biological activity of the substance is now being determined. A more detailed account of this work will appear at a later date.

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## Large Scale Paper Chromatography

**Charles Yanofsky, Elga Wasserman, and David M. Bonner**

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In view of the excellent separation of microquantities that can be achieved by paper partition chromatography (*1*), an attempt has been made to apply these same principles on a larger scale.

Two obstacles were encountered initially in large scale chromatography, the first being the difficulty of applying several milliliters of solution to a sheet of paper in a narrow straight band, and the second, obtaining a thick paper which could handle large quantities and still give good separation.

Attempts to apply several milliliters of solution from a capillary by hand were unsatisfactory, since it was virtually impossible to maintain a narrow band. It was found, however, that the application of solutions to paper could be greatly facilitated by the use of an automatically revolving drum to which the paper could be attached. The liquid could then be fed onto the paper, using a narrow capillary tube.

Such an apparatus can be readily set up in the laboratory using a kymograph, modified as shown in Fig. 1. The lower drum (A) of the kymograph is fixed at any convenient height by means of the latch (G). A second drum (B) is then put onto the shaft above (A), but is separated from (A) by means of a one-hole rubber stopper (C) which serves to provide a 1½-in. clearance between the two drums. This is desirable in order to prevent blotting between the paper and the drum when liquid is applied to the paper. A sheet of Whatman No. 1 paper, 17 in. high and 20 in. wide, is wrapped around the drums and fastened by means of two elastic bands. These can be closed most readily and held tightly around the paper if hooks and eyes are sewn on the ends. The paper is fastened in such a way that it overlaps in a direction opposite to that of the rotation of the kymo-

graph. Its lower edge should reach about 1 in. below the gap between drums (A) and (B).

The capillary (F) is clamped on a ring stand by means of a cork, as shown, so that the slightly bent tip of the capillary is pressed against the paper. The tip must be fire-polished to prevent scratching of the paper. The kymograph is then set in rotation and the solution to be

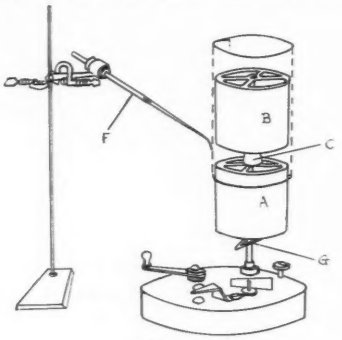


FIG. 1.

applied is added to the capillary tube. Unless this solution is absolutely free from solid particles a small cotton plug should be inserted in the capillary to serve as a filter. A heat source is used to facilitate evaporation of the solvent. A 250-watt infrared lamp has been found useful for this purpose. The band width is determined by the rate of flow of the solution, and may be regulated both by the size of the capillary opening and the speed of rotation of the kymograph. Flow rates can also be readily varied by applying gentle air pressure to the capillary.

By this method it has been possible to apply a 5-ml fraction of a methyl alcohol solution to a sheet of Whatman No. 1 paper in less than 15 min, and at the same time maintain a narrow band of material. The amount of any substance which should be applied in this manner is, of course, ultimately limited by the sharpness of the separation which can be obtained on the paper, and will vary in each case.

After the paper is dry and removed from the drum, any standard method can be used for developing the chromatogram. The authors have found it suitable to cut the sheet into two sections, 13 in. and 7 in. wide, respectively. These can then be stapled into two cylinders, which are simultaneously developed as ascending chromatograms in a glass-covered cylinder, 6 in. in diam and 18 in. high, containing 100 ml of developing solvent. A small section of the developed chromatogram is cut off lengthwise and used in order to detect the position of the desired substance if its $R_f$ value is not already accurately known. Once this has been ascertained, the entire desired section of the paper can be cut out and the material eluted by shaking with successive portions of an appropriate solvent, or by treating the paper with the solvent in a Waring Blendor.

Many different thick filter papers have been tested for suitability in the separation of larger amounts of material. The most satisfactory paper tested so far is Schleicher and Schuell paper No. 470-A[1] (0.025 in. thick). The separation on this paper is not as good as on thinner paper, but has proved very satisfactory for the initial separation of large amounts of material.

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## Relationship in Mice of Intestinal Emptying Time and Natural Resistance to Pig Ascaris Infection

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Rapid intestinal emptying time of young mice is involved in their high degree of natural resistance to the cestode, *Hymenolepis nana* var. *fraterna* (*1*). This emptying-time factor also appears to be operating in the distribution of *Trichinella spiralis* in the intestinal tracts of mice (*3*). It was, therefore, of considerable interest to learn from preliminary experiments that young mice, as compared with guinea pigs, have a remarkable degree of natural resistance to infection with pig ascaris (*Ascaris lumbricoides suum*). The aim of the present study is to determine the relationship of intestinal emptying time and natural resistance to infection for this parasite in mice.

The first three experiments were carried out using female mice, two months old, to establish the minimal infecting *Ascaris* egg dose. The methods of obtaining mature embryonated eggs and infecting the animals have been described earlier (*2*). One half of the mice in each egg-dose group were sacrificed between the fifth and eighth day after attempted infection so as to observe grossly the appearance of the lungs and to search for migrating larvae in that organ. This determination was qualitative only and was made by pressing small pieces of the entire lungs between two glass slides. These slides were examined microscopically with 100 × magnification. The remaining half of the mice were observed daily for 20 days to establish survival rates.

In the first experiment, the mice were divided into five groups of six mice each. Those of group 1 received 600 eggs. This dose for each succeeding group was increased by 600 so that the mice of the last group, group 5, received 3000 eggs. None of the mice showed outward evidence of infection, and of those autopsied the lungs appeared normal and were negative for larvae by the

[1] The author acknowledges with appreciation the technical assistance of Miss Dolores Stough during a portion of the study.

[1] Sample sheets of this paper were kindly furnished by the Carl Schleicher and Schuell Company of New York City.

microscopic method described. In experiment 2, seven groups of four mice each were used. In this case the egg dose for the mice of group 1 was 3600. This was increased by 1200 in each succeeding group so that the animals of group 7 received 10,800 eggs. The results were the same as for experiment 1. In experiment 3, seven groups were used, each with four mice. Those of group 1 received 12,000 eggs. This dose was increased by 3000 in each succeeding group, so that the mice of the last group, group 7, received 30,000 eggs. Except for group 7, the results were identical with those of experiments 1 and 2. The two mice of group 7 autopsied six days after infection showed a few hemorrhagic spots on the surface of both lungs; 15 and 25 larvae, respectively, were observed in pressed lung sections. The remaining two mice of group 7 were in apparent good condition 20 days after infection.

Although the number of animals was small, the results suggest that an egg dose of about 30,000 is the minimal infecting dose for mice. This agrees with the minimal dose used by Sprent and Chen (*4*) in a recent study. Thus, mice have a strong natural resistance to infection with this parasite, as compared with guinea pigs, which can be infected with egg doses as low as 6600 (*2*).

Experiment 4 was also performed with female mice two months old, to determine whether the rapid intestinal emptying time of mice of this age (*1*) is a factor in their striking resistance to infection as demonstrated in experiments 1–3. The method of artificially slowing the emptying time of experimental mice with 1% morphine sulfate was the same as that used in an earlier study (*1*). Sixteen of the mice were divided equally into experimental and control groups. The morphine was injected into the experimental animals, and 15 min later all of the mice were given 12,000 eggs, or less than one-half the established minimal infecting dose. The effectiveness of morphine in slowing the intestinal emptying time was verified by determining the passage of carbon ink in three additional mice (*1*). Six days after infection, one half of the experimental and control mice were sacrificed. The lungs of the controls appeared normal, and no larvae were found in pressed sections. This was expected from the results of experiment 3. However, three of the four mice given morphine sulfate prior to infection showed considerable lung hemorrhage, and an average of 150 larvae was observed. The remaining four mice of the control group showed no outward evidence of infection during the 20-day observation period. On the other hand, one of the remaining four experimental mice died on the ninth day of infection, apparently from lobular pneumonia caused by the larvae. The other three mice of this group, although showing signs of respiratory involvement, survived the infection.

It is clear from results of experiment 4 that mice given morphine sulfate as described were rendered considerably more susceptible to infection with *Ascaris* eggs than untreated controls given the same number of eggs. In fact, the drugged mice appeared to be more heavily parasitized than the nondrugged mice in experiment 3, which had been given more than twice as many *Ascaris* eggs. Other factors in this resistance may be affected by morphine, but the most reasonable explanation for increased susceptibility of drugged mice is the reduced intestinal emptying time, which presumably allows greater numbers of eggs to hatch than in control animals. Thus, the rapid intestinal emptying time of young mice is probably an important factor in their strong resistance to initial infection with pig ascaris, as was demonstrated earlier for natural resistance to *Hymenolepis* (*1*).

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## Electrometric Titration of Some Functional Groups


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Although simple titrimetric methods are available for quantitative analysis of many different types of inorganic compounds, relatively few organic compounds lend themselves to rapid volumetric analysis. Carboxylic and amino compounds, which can be titrated because of their

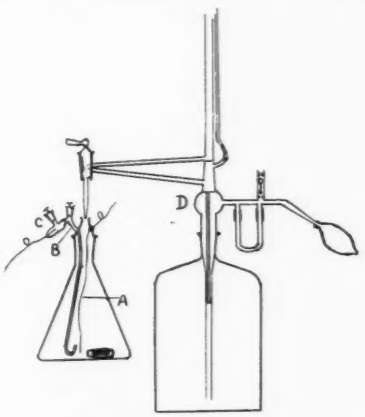


Fig. 1. Schematic drawing of the apparatus.

acid-base property, and olefinic compounds, which can be determined by iodine or bromine titration, represent the main types of organic compounds usually assayed volumetrically. A brief description is given in this preliminary report of a relatively simple electrometric method for the volumetric analysis of several functional groups

[1,2] Fellows, American Foundation for Pharmaceutical Education.

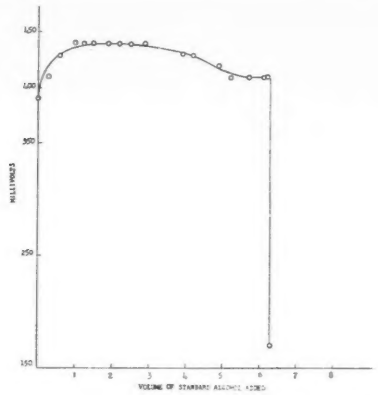


FIG. 2. Electrometric titration of isobutyl alcohol.

including $-OH$, $-NH_2$, $R_2CO$, RCHO, $RCO_2R$, and other easily reducible groups based on $LiAlH_4$ titration.[3]

The apparatus used, shown in Fig. 1, consists of a silver electrode *A*, salt bridge *B*, an isolated silver electrode *C*, and an automatic burette *D*. Dried and purified tetrahydrofuran is used to fill the salt bridge and the isolated electrode chamber, LiBr being employed as the electrolyte in both cases. In addition, a small amount of iodine is added to the electrode chamber to act as a depolarizer. The potential of the electrical cell is most conveniently followed by an indicating potentiometer such as Beckman Type H pH meter.

TABLE 1

ELECTROMETRIC TITRATION OF ISOBUTYL ALCOHOL

| Wt of sample in g | Ml of alcohol sol.* | | | Moles of alcohol | | |
|---|---|---|---|---|---|---|
| | Run | Blank | Diff. | Present | Found | % error |
| 2.653 | 6.30 | 16.70 | 10.40 | 0.0359 | 0.0358 | 0.3 |

* Ethyl alcohol 20.00% by volume.

The procedure employed is as follows. A weighed sample of approximately 1 g of the unknown substance to be analyzed is introduced into the reaction vessel. Fifty ml of pure tetrahydrofuran and 20 ml of a solution of $LiAlH_4$ in tetrahydrofuran are added in turn and allowed to stand for a few minutes. The excess hydride is determined potentiometrically by adding a standard solution of ethyl or propyl alcohol in dry benzene. The end point is indicated by a sharp change in the voltage of the electrical cell. The difference between the amount of alcohol consumed during this back titration and that used during a blank run made without the sample represents stoichiometrically the amount of substance in the sample capable of reacting with $LiAlH_4$.

Typical results are shown in Fig. 2 and Table 1. In calculating the molar concentration of various functional types other than an alcoholic hydroxyl, it must be kept in mind that $-OH = -NH_2 = R_2CO = RCHO = -CO_2R = \frac{1}{2} - CO_2H$.

More complete details on the development and application of the titrimetric method described will be presented shortly in another publication.

[3] The use of $LiAlH_4$ for quantitative determination of various functional groups is not new. Hochstein (*1*), Zaugg and Horrom (*3*), Krynitsky *et al.* (*2*), and others have described gasometric methods analogous to the Zerewitinoff method based on measurement of hydrogen gas liberated by the sample on reaction with the hydride. These are, however, not true volumetric methods where a standard solution is added to a stoichiometric end point indicated by some visual or electrical change.

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## Quantitative Evaluation of Gomori Histochemical Preparations[1]

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Several of the histochemical methods for the demonstration of enzyme activity, which have been developed by Gomori, result in the localized deposition of an insoluble sulfide. The present method permits the quantitative estimation of the enzymatic activity represented in such microscopic sections. There are theoretical and practical objections to methods based on visual or photometric measurement of the blackening (sulfide) as deposited in the section. In the present procedure, the sulfide in a section is extracted and converted to methylene blue by a modification of the method of Fogo and Popowsky (*1*), and the methylene blue in solution is then measured photometrically. The method does not permit comparison between localized areas in any one section unless these are excised, but it will give a measure of differences between separate sections. As given, the procedure deals with volumes 1000 times smaller than those described by Fogo and Popowsky, but the reaction is so sensitive that intermediate scales of volume will serve for most histological preparations.

*Procedure.* Paraffin sections are placed at the bottom of small (6×50 mm) test tubes and deparaffinized with benzene, rinsed with acetone, and dried in air. The section should lie flat against the glass tube without folds. A section previously used for microscopic study is suitable if transfer from the slide to the test tube can be accomplished without loss.

The Gomori substrate as used for microscopic preparations is added and the section incubated for the same period of time as an adjacent serial section, prepared on a slide for microscopic examination. (Sections for mi-

[1] This work was aided in part by a grant from the Dr. Wallace C. and Clara A. Abbott Memorial Fund of the University of Chicago.

eroscopy are mounted dry on albumin-coated slides to avoid destruction of some of the enzyme which occurs when water is used to flatten paraffin sections). The enzymatically liberated phosphate is converted to the lead salt, and the usual treatment with ammonium sulfide and careful rinsing with water follows. It is necessary to substitute lead for the cobalt of the alkaline phosphatase procedure, since cobalt sulfide is insufficiently soluble in the HCl required subsequently.

TABLE 1

| Duration of incubation (hr) | Optical density of methylene blue* | μg Sulfide (approx.) | μg Sulfide†/hr since previous determination |
|---|---|---|---|
| 0.5 | .60 | .195 | |
| 1.0 | .75 | .244 | .098 |
| 2.0 | .94 | .305 | .061 |
| 4.0 | 1.21 | .393 | .044 |
| 6.0 | 1.48 | .480 | .044 |
| 8.0 | 1.64 | .530 | .025 |

* Final volume 277 μl.

† Includes sulfide derived from preformed (nonenzymatic) phosphate.

To the tube containing a dry section stained with lead sulfide, there is added 135 μl of water and 25 μl of a solution of 0.1 g *p*-amino dimethyl aniline sulfate (Eastman Kodak Company) in 100 ml of 5.0 *N* HCl. After standing 20 min with occasional stirring to achieve solution of the sulfide, there is added 5 μl of 0.023 M ferric chloride in 1.2 *N* HCl. This is stirred and allowed to stand for 20 min and the methylene blue is determined in a spectrophotometer at 670 mμ using microcuvettes. For larger or heavily stained sections, final volumes of 3.0 ml may be more suitable. Appropriate lead sulfide standards are also prepared.

*Experiments.* Serial sections of rabbit appendix 10 μ thick and 14 sq mm in area were incubated in Gomori glycerophosphate substrate for alkaline phosphatase pH 9.5 for from ½ to 8 hr at 26° C. Microscopically, this gave a range from faintly stained sections at ½ hr to generalized overstaining after 8 hr. The amount of sulfide found after the various periods of incubation is shown in Table 1. From the table it is evident that in this material the rate of deposition of sulfide decreased appreciably after 6 hr of incubation under these conditions. Both the amount of sulfide formed and the time scale of decrease in enzymatic activity are in fair agreement with expectation based on independent quantitative microestimations under standard quantitative conditions.

The method should be applicable to any of the histochemical procedures involving deposition of a sulfide soluble in hydrochloric acid.

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## Comparison of Electroencephalographs of Young Rats from Dams on Synthetic and on Normal Diets[1]

**M. D. Overholser, J. R. Whitley, B. L. O'Dell, and A. G. Hogan**

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Richardson and Hogan (*1*) observed hydrocephalus in young rats born of dams on a synthetic diet, and concluded that the abnormality was due to a deficiency in the maternal diet. Young rats with the same nutritional history, though free from any sign of hydrocephalus, learn their way through a maze more slowly than do those from the stock colony (unpublished data). In a search for other differences between these two groups of rats, their electroencephalographs were compared. There were no significant differences; however, since to our knowledge observations of this kind on the rat have not been published, it seemed desirable to have a typical electroencephalograph of this animal described in the literature.

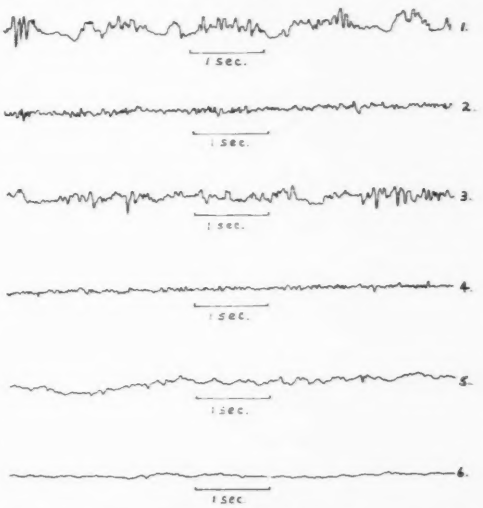


FIG. 1. Electroencephalographs of a normal rat from dam on the stock diet, a rat from dam on the synthetic diet and a hydrocephalic rat from dam on the synthetic diet. 1—Lead I, and 2—Lead II; normal rat from dam on the stock diet. 3—Lead I, and 4—Lead II; rat from dam on the synthetic diet. 5—Lead I, and 6—Lead II; hydrocephalic rat from dam on the synthetic diet.

Fifty-seven young rats, 4–8 weeks of age, from dams on the synthetic diet, were paired according to age, weight, and sex with an equal number from dams on the stock diet. They were given an intraperitoneal injection

[1] This investigation was supported in part by a grant from the U. S. Public Health Service.

of avertin (0.01 ml/g of body weight), their heads were shaved, and silver electrodes (3 mm in diam) moistened with electrode paste were attached to the skin with collodion. Two leads were taken from each animal. In Lead I, the first electrode was placed in the midline of the skull on a line between the external auditory meatuses; the second electrode was placed in the midline 12 mm in front of the first electrode. In Lead II, both electrodes were placed on the line between the external auditory meatuses, each one being 6 mm from the midpoint. The recordings were made with an Offner amplifier (type 140) and crystograph set at a speed of 2.5 cm/sec.

TABLE 1

FREQUENCY OF BRAIN WAVES IN THE RAT

| No. of rats | Diet of dams | Average frequency per sec | |
|---|---|---|---|
| | | Lead I | Lead II |
| 57 | Stock | 30.8 | 32.4 |
| 57 | Synthetic | 30.2 | 31.9 |
| 3* | Synthetic | 28.0 | 29.0 |

* Hydrocephalic rats.

A typical record from each group is shown in Fig. 1. The frequency per second was the measurement used in the analysis of the records. All countable waves were included and an average was taken of several counts on each recording. There was no significant difference in the frequency of the brain waves of the two groups of rats from dams on different diets, but the average frequency for three animals with well-developed hydrocephalus was somewhat lower than is normal. These results are shown in Table 1.

**Reference**

1. RICHARDSON, L. R. and HOGAN, A. G. *J. Nutrition*, 1946, **32**, 459.

## Studies on the Life Cycle of *Syphacia obvelata*, a Common Nematode Parasite of Rats[1]

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*Syphacia obvelata* is an oxyurid nematode frequently occurring in the ceca of laboratory and wild rats and mice. It has been reported once from man (*4*). Considering its common occurrence and wide distribution, surprisingly few details are known regarding its life cycle. It has been assumed that this cycle is simple and direct, and that rats are infected from eggs in feces. The worms occur, usually in large numbers, in the cecum. Males and immature females are found most numerous in the tip of the cecum, although a few may be found in other parts of the cecum and in the large intestine. Gravid females are found throughout the cecum and large intestine, including the rectum. I have also collected them from washings of the body surface of the anal region. In scores of autopsies, there was no evidence that eggs are ever laid within the host. Repeated search, using a variety of the usual laboratory methods, revealed no eggs in the feces, although Philpot (*3*) found a few in the feces of mice. Lawler (*2*) seemed able to infect mice by feeding them with macerated gravid female worms from infected mice, although the number of mice used was small. He did not mention any period of incubation. Using *S. obvelata* from rats, I have not been able to infect rats by this method.

Attempts to infect rats by feeding whole gravid female *Syphacia*, freshly collected from an infected rat, were unsuccessful. The test rats used were previously treated with phenothiazine or carbon tetrachloride to rid them of any natural infection that might be present. Tests show that both of these drugs are effective anthelmintics. Attempts to infect rats by feeding eggs liberated from gravid female *Syphacia* were also unsuccessful. Finally, although it was impossible to demonstrate eggs in the feces of rats proved by autopsy to be heavily infected, feces from infected rats were fed to test rats. No infections resulted.

Several methods of incubating eggs to the fully embryonated, infective stage were tried. The eggs did not develop well in distilled water, tap water, or dilute formalin solutions, either at 20° or 37° C. Eggs were also cultured in moist air, as recommended by Deschiens (*1*). None of these methods produced eggs that were infective to test rats.

All these negative results led to the discovery of the natural location of embryonated eggs and the probable means of transmitting the infection. A rat was lightly anesthetized to prevent struggling, and its anal region was washed with 10% alcohol. The washing was caught in a glass container. This liquid was then centrifuged and the sediment examined. A fairly large number of embryonated eggs and some larvae measuring 0.14–0.22 mm in length were obtained in this way. In addition to unhatched embryonated eggs found on the anal region, about 25% of the eggs found were actually empty egg shells. Using water in place of the 10% alcohol, living larvae as small as 0.09 mm in length have been recovered. Whether the variation in size of what must be recently hatched larvae is due to swelling or to growth is not known at present. Thus eggs are liberated from the worms, become embryonated, and may hatch on the body surface of the anal region. Other rats may become infected by licking these embryonated eggs or the larvae from the body of an infected rat. Another possible method of infection is through the anus. Schüffner and Swellengrebel (*5*) showed that some eggs of *Enterobius vermicularis*, the human pinworm, hatch on the anal region of the host, and that some larvae may migrate back into the body through the anus and rectum, a method of infection which they termed "retrofection." Careful examination of the posterior inch of the large intestine

[1] Studies from the Department of Zoology, University of Nebraska, No. 242. The work was done under the direction of Dr. H. W. Manter.

was made on eight infected rats. In one of the rats, seven living larvae were found in this region. All were about 0.2 mm long, or only slightly larger than the size (approximately 0.17 mm) Philpot reported for recently hatched larvae, and within the range of sizes of larvae found on the body surface. In another rat, one small larva and three gravid females, the latter probably moving to the outside, were found in this region. These findings suggest that retrofection does occur in the life cycle of *S. obvelata*. It is possible such infection occurs in many oxyurids. It would explain the massive infections sometimes found, for example, in reptiles.

In summary, gravid females of *S. obvelata* migrate from the anus of the host; eggs are deposited, either by being laid or by rupture of the body of the female worm, on the skin of the anal region; here the eggs become fully embryonated and at least many of them hatch; recently hatched, living larvae have been recovered not only on the body surface of the anal region but also in the posterior portion of the large intestine. These findings indicate that infection with *S. obvelata* can occur by larvae entering the anus, that is by retrofection, as recently described for *Enterobius vermicularis*. Infection by mouth by licking infective eggs or larvae from the skin probably also occurs and must be the method whereby young rats acquire infection from an infected mother.

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2. Lawler, H. J. *J. Parasitol.*, 1939, **25**, 442.
3. Philpot, F. *J. Helminth.*, 1924, **2**, 239.
4. Riley, W. A. *J. Parasitol.*, 1920, **6**, 89.
5. Schüffner, W. and Swellengrebel, N. H. *J. Parasitol.*, 1949, **35**, 138.

# *Comments and Communications*

## The Donora Episode

One year ago 20 persons lost their lives at Donora, Pennsylvania, in America's first mass killing from industrial air pollution. Now the U. S. Public Health Service has released a preliminary report on its year-long study of the Donora tragedy. This represents the Public Health Service's first foray into the field of community air pollution. Two years ago they were not even interested in making a small grant to help studies already well along in opening up this health field. Today they suddenly find the field so important that they quickly request $750,000 from Congress to enlarge upon their studies! Just what did their year's work, with a staff of 25 investigators, show?

They found that 42.7% of the people living in the Donora-Webster area were affected in the poison smog of a year ago. The quick survey made by local Donora workers at our request soon after the tragedy showed 43.2%. They found—as did we—that the percentage affected rose rapidly with age, was greatest at higher levels than down along the river, and was highest across the river in Webster. They found in the valley air the same irritants to the respiratory tract that were pointed out in our December report, but they found no dangerous concentrations and hence were unable to identify the killing agent.

The most valuable part of their year's work—analysis of poison output from the steel and zinc plant stacks—remains unused and unevaluated in their written report. They spent months analyzing the valley air for poisons, but failed to calculate the concentrations probably present during the killing smog a year ago, when an inversion blanket clamped a lid down over the valley's unfortunate people. Had they made such calculation, they would have found that even one day's accumulation of the very irritating red oxides of nitrogen from the acid plant stacks would have caused concentrations almost as high as had been set as the maximum allowable for safety of factory workers exposed only for an 8-hour work day. At the end of 4 days of last year's blanketing smog, concentrations reached were probably more than four times higher than the 10 milligrams per cubic meter of air listed as the upper limit of safety! And the Donora people breathed the poisoned air not 8 hours a day but for 4 whole days. *More than 4 tons* of this poison gas were poured out into the valley air every day during the April test period, even though the brownish-red plumes from the acid plant stacks were then very much less dense than those commonly seen up to the time of the October tragedy.

Stack output of zinc and the sulfur oxides were also found much too high for safety under smog conditions, while the amounts of carbon monoxide emitted were enormous. Because accumulation in the valley air of all carbon monoxide emitted over a 4-day period would probably have been fatal to the whole population, and because no signs of carbon monoxide poisoning were evident in Donora at any time, the Public Health Service investigators concluded that it would be unjustifiable to clamp a hypothetical lid down over the valley. This was a serious error on their part, for their own report (meteorology section) showed a gentle southward drift of the valley air throughout the critical part of the October smog period. Ninety percent of the carbon monoxide arose from blast furnace stacks located at the extreme southern end of the town and was thus carried away from the Donora residents. This gentle southward air movement also accounted for the same high illness rate throughout all parts of Donora as prevailed in its northern edge alongside the zinc plant.

There are now available up-to-date methods of cleansing such stack gases of harmful materials and the burning of the carbon monoxide on to carbon dioxide should be considered as a fuel-saving measure in plant economy. The operators of the Donora zinc smelter and sulfuric acid

plant should have taken warning at the time of the Belgian disaster of 1930, when 60 persons lost their lives and many thousands were made ill under conditions almost identical with those at Donora. Yet, almost two decades later, the outmoded smelter at Donora was still operating as it and its Belgian counterpart were doing in 1930. Let us hope that the Donora tragedy may prove such an object lesson in air pollution dangers that no industrial plant will feel safe in the future in pouring aloft dangerous amounts of poisonous materials. Furthermore, safety standards to be set up should be those that will give safety under the most adverse weather or smog conditions.

The U. S. Public Health Service investigation of animal deaths in the surrounding countryside was merely cursory, and the report fails to consider at all the terrible devastation and erosion that have resulted from the killing of nearly all plant life within more than a mile radius of the zinc smelter. Surely these were important features of the local air pollution problem. The Federal Security Administrator and the Surgeon General (in their forewords to the report) claim that the Service has here opened up a *new* field in the nation's health, blandly ignoring the years of work others had put in.

Let us hope that the Donora disaster will awaken people everywhere to the dangers they face from pollution of the air they must breathe to live. These 20 suffered only briefly, but many of the 6000 made ill that night will face continuing difficulties in breathing for the remainder of their lives. Herein lies the greatest health danger from polluted air—continuing damage to the respiratory system through years of nonkilling exposure.

Millions of Americans and most medical scientists had been aware of this important public health hazard for several years before the Donora episode spotlighted the community dangers of industrial air pollution. But the U. S. Public Health Service focused its interest on the health of workers *within* the plants. Only after the Donora disaster was it drawn into the much more important aspect of the problem—the relation of industrial air pollution to *community* health.

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## Correction

In reference to the article "Chromatographic Analysis of a Mixture of Proteins from Egg White" (*Science*, 1949, **110**, 564), the cation exchange resin Dowex 50 employed in the experiment cited was obtained in February, 1949, from the Microchemical Specialties Company, Berkeley 3, California, under the name of Ion-X, and not from the Dow Chemical Company as reported in the footnote. We have thus far not obtained satisfactory results with a sample of Dowex 50, (24427), obtained from the Dow Chemical Company on August 8, 1949.

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## Molecular Orientation and Intracellular Photometric Analysis

In two recent articles B. Commoner and D. Lipkin (*Science*, 1949, **110**, 31, 41) have questioned the validity of the microspectrographic techniques of the sort originated by Caspersson, whereby quantitative estimates of chemical constituents of cells are obtained from measurements of absorption with a microscope and suitable photometric apparatus. Although the main emphasis is placed upon the possible influence of molecular orientation upon measurements of ultraviolet light absorption by nucleotides, it is the conclusion of Commoner and Lipkin that "the entire problem of interpreting intracellular extinction measurements needs to be reexamined with the realization that one is dealing not with true solutions but with oriented aggregates of molecules." It is worth noting that the criticism did not arise from the authors' observation of an effect of orientation upon absorption. It is, rather, based upon inferences from certain physical principles, from the meager information as to the structure of nucleic acid molecules, and from a particular interpretation of selected data on ultraviolet absorption published by Caspersson and his students.

In this laboratory we have been making photometric studies of fixed cells, measuring not only the natural ultraviolet absorption but, in addition, the absorption of the following: (a) the Feulgen reaction, in which color is restored to Schiff's decolorized fuchsin reagent by the aldehyde group of desoxyribose; (b) methyl green staining, in which a basic dye of the triphenyl methane group is combined with the phosphoric acid of desoxyribose nucleic acid (Pollister, A. W. and C. Leuchtenberger, 1949, **35**, 111); and (c) the Millon reaction for protein, in which new chromophores are produced, apparently as derivatives of the phenolic group of tyrosine and tryptophane. Our measurements would seem to have been made under conditions very favorable for showing any effect of molecular orientation upon absorption, since they are all on fixed preparations in which, as T. Caspersson pointed out in 1940 (*Chromosoma*, 1940, **1**, 605), the dehydration and shrinkage of standard cytological technique tend to increase birefringence. Moreover it may be added that the senior author has noted that dehydration of precipitated nucleohistone fibers enormously increases their negative birefringence. Yet, in spite of these favorable conditions, in thousands of measurements there is no case (with the possible exception of some anomalous data on striated muscle) in which the data can be readily interpreted, by the criteria Commoner has set forth, as evidence for an effect of molecular orientation on absorption. As will be described below: (a) the distribution curves are symmetrical at all extinction values, not tending to cluster near 0.3; (b) Lambert's law, that extinction is proportional to thickness, has been repeatedly shown to hold for measurements of nuclei, cytoplasm, and intracellular substance; (c) there is good evidence that extinction varies directly with the concentration for the Feulgen nucleal reaction and for ultraviolet absorption of at least some living cells; and (d), as expected from the above, we

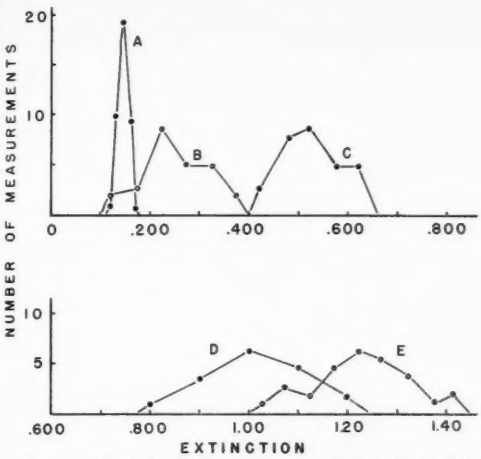


FIG. 1. Typical distribution curves of photometric data. A—Sections of nucleoli, corn pollen mother cells, Millon reaction, 365 mμ. B—Nuclei of mouse sarcoma (fresh tumor tissue), methyl green, 625 mμ. C—Sections of nucleoli, corn pollen mother cells, 254 mμ. D—Mouse primary spermatocyte nuclei, Feulgen reaction, 557 mμ. E—Preleptotene nuclei from mouse testis, Feulgen reaction, 557 mμ.

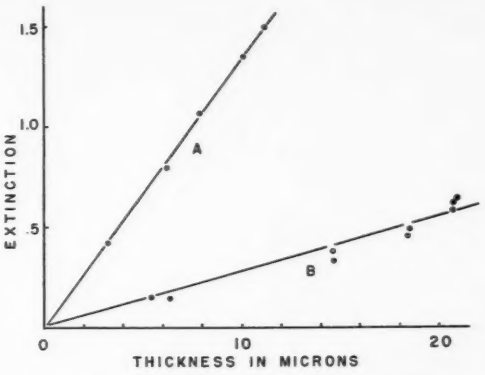


FIG. 2. Demonstration of the direct relation between extinction and thickness of absorbing material (Lambert's law). A—*Ambystoma* liver nuclei, cut at various thicknesses, Feulgen reaction, 30% formalin fixation, 557 mμ. Each point represents the mean extinction on ten nuclei. B—Living grasshopper spermatocyte, 257 mμ, replotted from Caspersson (*Chromosoma*, 1939, **1**, 147, Fig. 7. Since none of the grasshopper nuclei studied in the paper is smaller than 10.0 μ in diameter, it is assumed that the scale on the abscissa of Caspersson's Fig. 7 should read 0–50 μ, instead of 0–5 μ).

have found in these materials that rotation of the polarizer has no effect upon absorption in visible light. Finally, it may be added that in our opinion the selected data used by Commoner, instead of supporting the view that orientation of nucleic acid is affecting absorption values, actually indicate the contrary and support what we have found.

In Fig. 1 are shown a number of typical distribution curves of extinction values. The values have been corrected for nonspecific light loss by subtraction of measured blanks in cases where such blanks absorbed significantly. Some populations are in a range entirely above 0.3, others entirely below, while one overlaps this expected limiting value which corresponds to 50 percent transmission. All of the curves show the sort of symmetry that is characteristic of a population varying in random fashion, like many biological samples or measurements with random errors. There is no hint of the operation of any special factor tending to depress the higher values or to cause marked distortion in the vicinity of 0.3. This same symmetry characterizes the curves Commoner has plotted from data of the Caspersson school (e.g., see his Fig. 4A).

Commoner points out that if there is an orientation effect, "then the value $E = 0.3$ tends to be limiting despite rather large variations in thickness of the materials studied." In other words, marked deviations from Lambert's law should result. Actually, in practice, it is so generally true that Lambert's law holds in cytological absorption work that often the absorption will detect thickness differences which are not readily apparent to visual inspection, and only become confirmed when thickness is carefully measured. Many simple experiments have served to point up this fact. For example, Caspersson described a demonstration that Lambert's law holds for the ultraviolet absorption of nucleic acid in living nuclei (*Chromosoma*, 1939, **1**, 147). He measured the absorption along various transects of a spherical spermatocyte nucleus, and showed that for each point the measured value was that expected for the thickness of the nucleus. We have replotted Caspersson's values (Fig. 2B), converting absorptions into extinctions. The curve shows no tendency to level off at 0.3, as would be expected if there were an orientation effect. We have made several similar demonstrations on nuclei. In a Feulgen-stained preparation we have measured a series of cylindrical nuclear plugs of decreasing radius, and found that, once the circumference is inside the peripheral zone of diffraction, the extinction rises in close approximation to expectation from the increasing optical path as the nuclear center is approached. Measurements of nuclear sections also show that Lambert's law is closely followed (Fig. 2A). That Lambert's law holds for the Millon reaction over a wide range of thicknesses (3 to 25μ) and extinctions (0.17 to 1.20) has been demonstrated by A. W. Pollister and H. Ris (*Cold Spr. Harb. Sympos. quant. Biol.*, 1947, **12**, 147).

In the preceding paragraph it has been shown that with the various methods which have been used in microscopic absorption studies, Lambert's law is followed with no indication of the influence of molecular orientation. It seems to us that this is convincing proof that in these cytological materials, if there is orientation of the chromophores of nucleic acid or protein or their derivatives, or dyes attached to them, this orientation has no measurable effect upon the relative absorption values. In other words, the Beer-Lambert law must be similarly uninfluenced by the orientation; for it seems self-evident

that if molecular orientation does not significantly affect the relationship between extinction and thickness of absorbing layer it cannot influence the relation of absorption to concentration in the same material. Therefore the photometric measurements should be capable of detecting changes in amount of absorbing material. There is good evidence that such changes can be detected. For example, losses of material from cells as a result of tissue extraction (Pollister, A. W. and Leuchtenberger, C. *Proc. nat. Acad. Sci.*, 1949, **35**, 66), enzymatic digestion (Pollister, A. W. and Leuchtenberger, C. *Nature*, Lond., 1949, **163**, 360), or of necrotic degeneration (Leuchtenberger, C. *Chromosoma*, in press) are thus readily picked up. The strongest proof of the real value of the cytological absorption technique comes from study of nuclei of varying chromatin content. It has long been known that nuclei of mammalian liver fall roughly into classes according to size, and it is generally accepted that these represent different degrees of polyploidy (Jacobj, W. *Arch. f. Entw.*, 1925, **106**, 124). For example, the three classes in the liver of the mouse and rat are presumably diploid, tetraploid, and octoploid. When these nuclei, stained by the Feulgen reaction, are measured photometrically, the computed relative values for desoxyribose nucleic acid fall close to the ratio 1 : 2 : 4.[1] The haploid nuclei of spermatids have close to one-half the amount of the smallest class of liver nuclei. We submit that such a correlation of calculated relative amounts with expectation from the presumed multiple of the basic amount of chromatin is highly unlikely to be obtained by photometric analysis if some extrinsic factor such as molecular orientation is operating to obscure the relationship between optical density, concentration, and thickness.

We have measured in polarized visible light (analyzer removed) fixed nuclei stained with either Feulgen or methyl green, from grasshopper (*Chortophaga*) testis, and from mouse liver and testis. We have found no evidence of dichroism in any of this material, although the sperm heads of the grasshopper are highly birefringent, and hence presumably have a high degree of molecular orientation. If the methyl green were bound in such a fashion as to reflect the orientation of the nucleic acid, a rotation of the polarizer have caused a detectable effect on the transmission, since crystals of methyl green are markedly dichroic.

Commoner (see his Fig. 2) cites the data which Caspersson reported for spermatocyte nuclei of various diameters as a case where absorption measurements "strikingly fail to follow the Beer-Lambert laws." Obviously this is a "striking failure" only if one assumes that the *concentration* of nucleic acid remains constant as the nuclear volume increases. Commoner has apparently overlooked the fact that Caspersson interprets his data very differently, as showing that in spite of some changes in nuclear size, at a given stage in meiosis *the amount of desoxyribose nucleic acid per nucleus remains nearly constant.* He showed this by calculations

[1] These data will be discussed in detail in a future paper by the junior author. Similar ratios have been obtained by Ris and Mirsky, *J. gen. Physiol.*, 1949, **33**, 125.

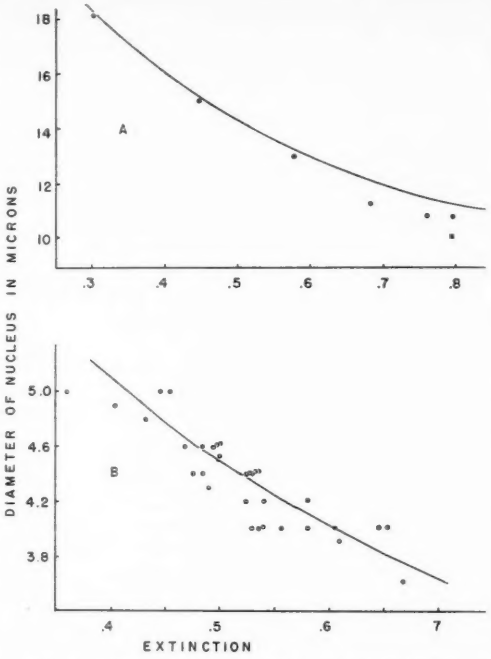


FIG. 3. Relation between nuclear size and extinction in two types of nuclei. Solid lines show the theoretical relation between diameter and extinction, assuming the amount of absorbing substance is constant per nucleus and the Beer-Lambert law holds. A—Living grasshopper spermatocytes, late leptotene, 257 mμ (data from Caspersson). B—Rat spermatid nuclei, Feulgen reaction, 557 mμ.

which appear in a column adjacent to the extinctions which Commoner has plotted. Since, in an earlier part of this paper, Caspersson had demonstrated that the Lambert law was closely followed for these very nuclei (see our Fig. 2B) it seems to us that, instead of being an example of failure of the Beer-Lambert law, these data indeed provide a striking demonstration of its validity for ultraviolet absorption of nucleic acid in these living nuclei. We have replotted Caspersson's data for the leptotene stage (Fig. 3A) to show that the extinctions follow what one would expect from varying concentrations of a constant mass of absorbing material. It has been our common experience in this laboratory that, as Caspersson first found, the minor size fluctuations of any type of nucleus (i.e., those differences which presumably do not involve any change in degree of polyploidy) are always accompanied by compensatory inverse changes of concentration of desoxyribose nucleic acid, as if the amount remained very nearly constant. An example is shown in Fig. 3B, from a population of haploid spermatid nuclei. If one is to explain such an inverse relationship of extinction to optical path as a failure of the Beer-Lambert law due to some obscure effect of molecular orientation, then one is forced to the unlikely assumption that this error seems always just

great enough to make the extinction at all volumes conform to the expectation if a constant amount of nucleic acid is being diluted as the nuclear volume increases. It may be added that this concept of the constancy of desoxyribose nucleic acid per nucleus is supported by recent evidence which has come from correlation of gross analyses with cell counts (Mirsky, A. E. and Ris, H. *Nature*, Lond., 1949, **163**, 666; Vendrely, R. and Vendrely, C. *Experientia*, 1948, **4**, 434). It is also consistent with the demonstration of the extraordinary stability of the desoxyribose nucleic acid fraction in interphase nuclei (Brues, A. M., Tracy, M. M., and Cohn, W. E. *J. biol. Chem.*, 1944, **155**, 619).

The positive evidence which Commoner has used to show that molecular orientation may have an important effect upon absorption values comes from his interpretation of the data which have been published by workers of the Caspersson school. Commoner restricts his selection to cases where the *area* measured is small, 1.0 μ or less because, "if the field is large, differences in the spatial organization of various areas included in it may obscure the orientation effect." Yet if material is so heterogeneous that one must, for measurement, select an area one μ or less in diameter to find approximate uniformity, how can it be expected that this small cylindrical mass will be homogenous through a section depth of 5 to 16 μ? From these selected data Commoner has plotted distribution curves, and has concluded that "The occurrence of several sets of measurements with well-defined maxima at 0.3 suggest that the orientation effect has probably influenced the values obtained." These significant maxima occur in three of his six curves, 4B, 4C, and 5. Of these, the last alone is probably plotted from values which are close to the actual 257 mμ absorption characteristic of the material. For only in this case have the extinctions been corrected for nonspecific light loss, which by the Caspersson method is computed by extrapolation from a part of the absorption curve which lies outside the region of specific absorption. In H. Hyden's paper on fixed nerve cells (*Acta Physiol. Skand.*, 1943, **6**, suppl. 17), from which the uncorrected extinctions of 4C have been plotted, the author has included with about one-third of the measurements a dispersion curve from which one can estimate the correction for nonspecific light loss. When this is applied to the extinctions of about 0.30, it reduces them to values ranging from 0.15 to 0.20. Thus the maximum for curve 4C is not 0.3 but somewhere near one-half of this. The data of 4B are likewise uncorrected, and from the shape of the accompanying curves it appears that the true mode must lie considerably below 0.3. Thus, of the six distribution curves only one (Fig. 5) actually shows a maximum near 0.3. Aside from the occurrence of this maximum there is little in curve 5 to support the view that the values have been influenced by molecular orientation. The extinctions do not cluster below 0.3, as expected from Commoner's theoretical curve 3B; instead they appear to be grouped fairly symmetrically about the mode, with, if anything, a slight preponderance of values slightly higher than the expected limit.

Commoner suggests that reorientation of the chromophores of nucleic acid may account in large part for the changes in ultraviolet transparency which accompany cell injury and death, and are such an obstacle to quantitative absorption studies on living cells. So far as we know, it has not yet been learned whether these are alterations in *specific light loss*, which could be influenced by chromophore orientation, or changes in *nonspecific* internal reflections and scattering (Caspersson, T. *Skand. Arch. Physiol.*, 1936, **73**, suppl. 8), which should be independent of orientation of the chromophores. There is qualitative evidence which suggests that most of the change in optical properties in dying protoplasm may be of the latter type. Students of living cells are familiar with the fact that in visible light, where there is no specific absorption, the most delicate criteria of cell injury are changes in the transparency of the protoplasm and an increase in the differences in refractive indices among the visible cell components. These should lead to marked changes in the amount of nonspecific visible light loss, and should, insofar as light scattering is involved, be enormously exaggerated in ultraviolet light.

The addition of the method of photometric analysis to microscopy marks one of the great forward steps in the study of cells. If this approach can be used to substitute objective relative values for such time-worn subjective cytological phrases as "more basophilic," and "less Feulgen-positive," then we truly have in our hands a powerful tool for the study of biology at the level of its characteristic microscopic unit, the single cell. It is important, however, that workers with these techniques become aware of all possible sources of error which may be constantly or sporadically present. Commoner and Lipkin have performed a useful task by calling our attention, in very explicit fashion, to one potential error which it would seem must become significant in some biological material. However, it does not appear that in most common cytological preparations the orientation of the chromophores of the constituent molecules has an appreciable effect upon the validity of absorption measurements.

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The foregoing comments of Pollister and Swift on the discussion by Dr. Lipkin and myself of certain aspects of microspectrophotometry are apparently intended to defend "the validity of the microspectrographic techniques of the sort originated by Caspersson." The authors may be assured that the *techniques* are not under fire from this quarter—a point which should be evident from the original papers.

Our papers deal rather with the validity of the widespread assumption that the Beer-Lambert laws may be applied with impunity to physical states as complex and dynamic as those encountered in living cells. The discussion was limited to the single case in which there are sufficient data relating to the optical properties of a natural

intracellular constituent to warrant any sort of analysis: the absorption of ultraviolet light by nucleic acids. The analysis led to the suggestion that, on the basis of present information, the assumption that nucleic acid concentration of cell structures is necessarily proportional to their extinction at 260 mμ is not a valid one.

Let us now examine the series of arguments made by Pollister and Swift in terms of their applicability to our basic proposition.

1) *That our discussion "did not arise from the authors' observation of an effect of orientation upon absorption."* This statement offers the reader a choice of either of two meanings. It may mean that Pollister and Swift find fault with our analysis because no observations of the effect of orientation of cellular materials on absorption have *ever* been made. If this is the case, their statement is inaccurate. As pointed out in our papers (*Science*, 1949, **110**, 34), such observations have been made by T. Caspersson (*Chromosoma*, 1940, **1**, 605). On the other hand, their remark may mean to imply that the discussion of the problem by Dr. Lipkin and myself is disqualified by the fact that we ourselves have never conducted such experiments. This unprecedented dictum would require the abandonment of a large part of science.

2) *That the papers were "rather, based upon inferences from certain physical principles. . . ."* The analysis of data by means of such inferences is so widespread as to merit at least some support on the basis of empirical success. If the practice were forbidden or frowned upon, among the first to suffer would be those who make applications of the Beer-Lambert laws.

3) *That studies in Pollister's laboratory show no evidence that various staining procedures and histochemical tests exhibit properties connected with orientation, i.e., dichroism, asymmetrical distribution frequencies, failure to follow Lambert's law.* Most of Pollister and Swift's commentary is concerned with this evidence, but as a reference to the title of the original discussion will show, it has no bearing on the question at hand. That such color reactions may be unaffected by the orientation of the material tested is clear from the experiment of staining crystalline tobacco mosaic virus inclusions with the Millon reagent. Although the crystal itself is dichroic in ultraviolet light, the Millon color shows no evidence of orientation in polarized light. A similar experiment is reported by Pollister and Swift themselves. This, of course, suggests that the orientation effect is not a problem in obtaining extinctions yielded by the colored groups produced in these staining procedures, but it does not constitute proof that extinctions due to nucleic acids are unaffected by orientation.

However, since the subject has been brought up, I may take this opportunity to suggest that the quantitative validity of the staining procedures cited by Pollister and Swift is open to doubt on other grounds. Some of the questions which require answers before these procedures may be said to conform with the elementary requirements of quantitative analysis are these: (1) Are the color-producing reactions stoichiometric? (2) Does the entire mass of the cellular material tested react with the reagent, or does the reaction take place only on the surface of microscopic or submicroscopic particles? (3) Does Beer's law hold for the conditions of the tests? There is considerable evidence (Ostwald, W. *Licht und Farbe in Kolloiden*. Dresden: Steinkopf, 1924. P. 308) that this relationship breaks down when the size of the light-absorbing particles approaches microscopic dimensions.

4) *That Caspersson* (Chromosoma, 1939, **1**, 147) *has demonstrated the validity of the Beer-Lambert laws by studying* (a) *the extinction of a grasshopper spermatocyte nucleus through transects of various thickness, and* (b) *the extinction of a group of such nuclei which have presumably swollen under the influence of ultraviolet irradiation without suffering a change in total nucleic acid content.* The actual data on which this criticism is based are these: (a) Fig. 7 of the paper published by Caspersson in 1939 shows a series of absorption measurements made through transects of various thickness of the nucleus of a single grasshopper spermatocyte. The values indicate that the extinction is proportional to the thickness at the point studied. According to the published scale of the abscissa of his figure, the nucleus had the improbable diameter of 2.1 μ, but Pollister and Swift claim that the scale is erroneous and that the value should be 21 μ. (b) In Table 1 of the same paper Caspersson reports the diameters, extinctions, and calculated nucleic acid contents of a series of spermatocyte nuclei in various stages of meiosis.

Pollister and Swift contend that the data listed under (a) constitute proof that Lambert's law holds for all the nuclei mentioned in (b). They make the further claim that the nucleic acid content per spermatocyte nucleus remains "nearly constant" in any given stage of meiosis. These two assertions are offered as support for the statement that "these data indeed provide a striking demonstration of its [i.e., the Beer-Lambert law's] validity. . . ."

Some exception can be taken to this deduction. Measurements on a single nucleus, plotted on a scale which needs to be reinterpreted by Pollister and Swift, seem but slender support for a conclusion of such moment. Furthermore, Caspersson's figure presents another difficulty which needs to be resolved: It shows a zero absorption in the cytoplasmic regions of the spermatocyte; yet photographs of similar cells published in the same study indicate significant cytoplasmic absorption.

Pollister and Swift state that I have overlooked that part of Caspersson's table which reports what they term the "nearly constant" values of nuclear nucleic acid content. Two errors of fact can be noted here. In the first place it would have been rather difficult to overlook this matter, since Dr. Pollister and I had a searching discussion of this table at the time that he was studying the first draft of my paper. Second, the value is far from constant. For the meiotic stage plotted by Pollister and Swift, Caspersson gives eight values, ranging from 20 to 26 mg $\times 10^{-9}$ of nucleic acid. For an earlier stage, included in the original table, but not plotted by Pollister and Swift, Caspersson reports five values, spread over the range 11.2 to 19.6 mg $\times 10^{-9}$ of nucleic acid. In these

data, one *might* envision a validation of the Beer-Lambert laws. The supporting evidence, however, is sufficiently flexible to allow considerable room for a difference of opinion.

5) *That the demonstration of Lambert's law is sufficient to rule out the possibility of deviations from Beer's law due to orientation phenomena.* This would considerably simplify the calibrations which must be made of many colorimetric reactions. Unfortunately, variations in concentration *per se* induce a number of intermolecular effects (including orientation) which can play hob with Beer's law. As cited in our original papers, this has been amply demonstrated by the work of Sheppard *et al.* Particularly pertinent is the well-known observation that with increasing concentration, solutions of tobacco mosaic virus will develop tactoid aggregates comprised of highly oriented particles. More prosaic but equally pertinent is the fact that concentration of salt solutions, for example, induces the formation of oriented aggregates (crystals) from a totally isotropic fluid.

6) *That the frequency distributions plotted in my paper show false maxima at the range* $E = 0.3$ *because a correction for nonspecific light losses was not applied.* Pollister and Swift state that to obtain the real extinctions due to nucleic acids, the dispersion curves shown by H. Hyden (*Acta Physiol. Skand.*, 1943, **6**, suppl. 17) in eight of his absorption spectra should be applied to all but one of the sets of data plotted by me, as well as to every value obtained by Hyden. Now on page 18 of his paper, Hyden states explicitly that dispersion corrections do not apply to tissues handled (as his were) according to the freeze-drying method of Gersh, unless they happen to have a large water content. He points out that the latter condition occurs in only a certain part of his material (representing eight values), and therefore the dispersion correction is applicable to these points alone. Furthermore, Pollister and Swift assume that "one can estimate the correction for nonspecific light loss" from Hyden's dispersion curves, and that this value can then be applied to all data which seem to lack such a corrective measure. This assumption neglects the fact that the correction factor, according to Caspersson, must be calculated from a series of extinctions in the range 300–350 mμ *determined at the precise area of the cell to which the correction is to be applied.* The dispersion curves are so variable that, for the eight cases which call for them, Hyden supplies individually determined corrections, even where two areas in the same cell are involved. There is therefore no basis for the indiscriminate application of a single correction factor to a wide variety of data.

One manifestly absurd result would be obtained by following the suggestion that a correction factor of about 0.15 be subtracted from all the extinction values not previously corrected by the authors. A significant portion of the values in each set of data (ranging from 10 to 50 percent) would be reduced to zero—or less. This would mean, for example, that about one-half of the chromosome regions studied by Caspersson (see *Science*, 1949, **110**, 37, Fig. 4E for frequency distribution) would appear to be totally devoid of nucleic acid.

7) *That a series of 35 sections of fixed nucleoli from corn pollen mother cells show a modal extinction value (at 254 mμ) well above 0.3 and therefore exhibit no evidence of the orientation effect.* It would be possible to agree that this evidence indicates that nucleic acid orientation is of no consequence in the single case of fixed nucleoli of corn pollen mother cells, if it were not for one disturbing factor—namely, nonspecific light loss. These data were obtained by determining the extinction at 254 mμ of nucleoli before and after treatment with trichloracetic acid at 90° C. The extinctions plotted in Pollister and Swift's Fig. 1C are presumably the differences between these two values. This procedure assumes, however, that the treatment of a nucleolus with near-boiling trichloracetic acid is so gentle as to make no appreciable changes in the intracellular structure which gives rise to nonspecific light losses. This assumption has yet to be given the support of experimental evidence.

It seems to me that certain current microspectrophotometric practices do not adequately reflect the fund of information that modern physical chemistry has placed at the disposal of biologists. One of the simple but vital lessons to be learned from the experiences of routine photochemistry pertains to the Beer-Lambert laws. Few analysts would choose to depart from the rule that any colorimetric reaction must first be calibrated with respect to known differences in concentration (and if necessary, sample thickness) before the extinctions yielded by unknown samples can be evaluated. More frequently than not, the result is a calibration curve which shows considerable deviation from the straight line called for by the laws of light absorption. If the monophasic systems of solution photometry involve such persistent departures from the Beer-Lambert laws, an equally cautious approach to the interpretation of extinctions obtained from cellular structures is called for. Such caution might have more than the negative value of preventing errors, for it could lead to a better understanding of the organization of matter that is peculiar to living things.

BARRY COMMONER

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# Scientific Book Register

ALLEE, W. C. *et al.* *Principles of animal ecology.* Philadelphia: W. B. Saunders, 1949. Pp. xii + 837. (Illustrated.) $14.00.

*Annual reports on the progress of chemistry for 1948,* Vol. XLV. London, W.1: Chemical Society, 1949. Pp. 379.

AVERY, GEORGE S., JR. (Ed.) *Survey of biological progress.* (Vol. 1.) New York: Academic Press, 1949. Pp. 396. (Illustrated.) $6.80.

BABKIN, B. P. *Pavlov: A biography.* Chicago, Ill.: Univ. Chicago Press, 1949. Pp. xiii + 365. (Illustrated.) $6.00.

BERANEK, LEO L. *Acoustic measurements.* New York: John Wiley; London: Chapman & Hall, 1949. Pp. vi + 914. (Illustrated.) $7.00.

BILLIG, HARVEY E., JR., and LOEWENDAHL, EVELYN. *Mobilization of the human body: Newer concepts in body mechanics.* Stanford, Calif.: Stanford Univ. Press, 1949. Pp. xi + 65. (Illustrated.) $2.00.

BONESTELL, CHESLEY, and LEY, WILLY. *The conquest of space.* New York: Viking Press, 1949. Pp. 160. (Illustrated.) $3.95.

BOOTH, HAROLD SIMMONS, and MARTIN, DONALD RAY. *Boron trifluoride and its derivatives.* New York: John Wiley; London: Chapman & Hall, 1949. Pp. ix + 315. (Illustrated.) $5.00.

BRAVAIS, M. A. *On the systems formed by points regularly distributed on a plane or in space.* (Trans. by Amos J. Shaler; Crystallographic Society of America, Memoir No. 1, 1949.) Pp. vi + 113. (Illustrated.) Order from: William Parrish, Crystallographic Laboratory, Philips Laboratories, Irvington-on-Hudson, New York. $3.90.

BRIDGMAN, P. W. *The nature of physical theory.* (Reissue.) New York: Dover Publs., 1949. Pp. 138. $2.25.

*British Pharmaceutical Codex 1949.* London W.C.1: Pharmaceutical Press, 1949. Pp. xxv + 1562. £3,3.

BROOKS, C. E. P. *Climate through the ages: A study of the climatic factors and their variations.* (Rev. ed.) New York: McGraw-Hill, 1949. Pp. 395. (Illustrated.) $4.50.

CHALMERS, BRUCE. (Ed.) *Progress in metal physics.* (Vol. 1.) New York: Interscience; London: Butterworths Scientific Publs., 1949. Pp. viii + 401. (Illustrated.) $9.50.

CHAPANIS, ALPHONSE, GARNER, WENDELL R., and MORGAN, CLIFFORD T. *Applied experimental psychology: Human factors in engineering design.* New York: John Wiley: London: Chapman & Hall, 1949. Pp. xi + 434. (Illustrated.) $4.50.

GUGGENHEIM, E. A. *Thermodynamics: An advanced treatment for chemists and physicists.* (Monographs on Theoretical and Applied Physics, Vol. II.) New York: Interscience; Amsterdam: North-Holland Publ., 1949. Pp. xxii + 395. (Illustrated.) $6.50.

GUTENBERG, B., and RICHTER, C. F. *Seismicity of the earth and associated phenomena.* Princeton, N. J.: Princeton Univ. Press, 1949. Pp. vii + 273. (Illustrated.) $10.00.

HEBB, D. O. *The organization of behavior: A neuropsychological theory.* New York: John Wiley; London: Chapman & Hall, 1949. Pp. xix + 335. (Illustrated.) $4.00.

PARKS, LLOYD M., JANNKE, PAUL J., and HARRIS, LOYD E. *Inorganic chemistry in pharmacy.* Philadelphia: J. B. Lippincott, 1949. Pp. x + 298. (Illustrated.) $6.00.

PATTY, FRANK A. (Ed.) *Industrial hygiene and toxicology.* (Vol. II.) New York-London: Interscience, 1949. Pp. xxviii; 535 + 1138. $15.00.

PLANCK, MAX. (Trans. from German by Frank Gaynor.) *Scientific autobiography and other papers.* New York: Philosophical Library, 1949. Pp. 192. (Illustrated.) $3.75.

RANDALL, H. M. *et al.* *Infrared determination of organic structures.* New York: D. Van Nostrand, 1949. Pp. v + 239. (Illustrated.) $10.00.

ROMER, ALFRED SHERWOOD. *The vertebrate body.* Philadelphia-London: W. B. Saunders, 1949. Pp. viii + 643. (Illustrated.) $5.50.

ROSSI, BRUNO B., and STAUB, HANS H. *Ionization chambers and counters: Experimental techniques.* (National Nuclear Energy Series, Div. V, Vol. 2.) New York: McGraw-Hill, 1949. Pp. xviii + 243. (Illustrated.) $2.25.

SEWELL, R. B. SEYMOUR. *The littoral and semi-parasitic Cyclopoida, the Monstrilloida, and Notodelphyoida.* (John Murray Expedition, 1933–34, Scientific Reports, Vol. IX, No. 2.) London (S.W. 7): British Museum of Natural History, 1949. (Illustrated.) 1£, 15 sh.

SHAND, S. J. *The study of rocks.* (Revised and enlarged 2nd ed.) New York: Macmillan; London: Thomas Murby, 1949. Pp. xi + 236. $2.50.

VALENTINE, WILLARD L., and WICKENS, DELOS D. (3rd ed.) *Experimental foundations of general psychology.* New York: Rinehart, 1949. Pp. xxi + 472. (Illustrated.) $3.00.

VON WEIZÄCKER, C. F. *The history of nature.* (English edition of *Die Geschichte der Natur* translated by Fred D. Wieck.) Chicago: Univ. Chicago Press, 1949. Pp. 191. (Illustrated.) $3.00.

WHELAND, G. W. *Advanced organic chemistry.* (2nd ed.) New York: John Wiley; London: Chapman & Hall, 1949. Pp. xi + 799. (Illustrated.) $8.00.

WINCHESTER, A. M. *Biology and its relation to mankind.* New York: D. Van Nostrand, 1949. Pp. ix + 777. (Illustrated.) $5.25.

YOUMANS, W. B. *Nervous and neurohumoral regulation of intestinal motility.* (Monographs in the Physiological Sciences.) New York-London: Interscience, 1949. Pp. ix + 129. (Illustrated.) $4.75.

# *NEWS and Notes*

**Merle A. Tuve,** director of the Department of Terrestrial Magnetism, Carnegie Institution of Washington, has been elected an honorary fellow of the Geophysical Institute, University of Alaska. Dr. Tuve was cited for his work in the field of electromagnetic wave propagation, his studies in nuclear physics, and his more recent contributions in the field of compressional wave propagation.

**Edmund Ezra Day,** chancellor of Cornell University, will retire January 31. He has been president of the university from 1937 until last July, when he became chancellor. The office of chancellor was created for Dr. Day when he submitted at commencement last June his resignation as president for reasons of health. A committee of six trustees and five faculty members has been appointed to review and recommend candidates for the presidency to the board of trustees.

**Louis A. Pardue,** University of Kentucky physicist, became chairman of the Council of the Oak Ridge Institute of Nuclear Studies on January 1. He succeeds **J. Harris Purks, Jr.,** who resigned from Emory University and the council to become associate director of the institute's General Education Board.

**Benjamin J. Birdsall,** who has been working with the Office of Foreign Agricultural Relations in its technical collaboration program with the western hemisphere republics, left the Department of Agriculture December 31 to serve as tropical agriculturist for W. R. Grace and Company.

**S. W. Frost,** on sabbatical leave from the Department of Zoology and Entomology, Pennsylvania State College, will sail February 10 to spend three months in Ecuador. He plans to collect insects from the coastal plain, the plateau area, and the upper Amazon Valley of Ecuador.

**John G. Kidd,** professor of pathology, Cornell University Medical College, and chief pathologist, New York Hospital, will deliver the 14th Christian Fenger Lecture of the Chicago Institute of Medicine and the Chicago Pathological Society on January 27, at the Palmer House, Chicago. His subject will be "Experimental Necrobiosis—A Venture in Cellular Pathology."

**Sidney P. Colowick,** associate professor in biochemistry, University of Illinois, has been appointed associate professor of biology at the McCollum Pratt Institute of Johns Hopkins University, effective January 1.

**Ralph E. Gould** retired December 30 after more than 31 years' service with the National Bureau of Standards, where he has been the chief of the Time Section for the past 26 years.

**A. A. Bitancourt,** director of plant biological research, Instituto Biologico, São Paulo, Brazil, became director general of the institute December 7, 1949. Dr. Bitancourt succeeds **H. da Rocha Lima,** who recently retired.

U. S. scientists invited by Centre National de la Recherche Scientifique to attend the symposium "Ferromagnetism and Antiferromagnetism," to be held at Grenoble July 3–7, include **J. H. Van Vleck,** chairman of the Physics Department, Harvard University; **N. M. Bozorth,** research physicist, Bell Telephone Laboratory; **Roman Smoluchowski,** associate professor of the Metals Research Laboratory, Carnegie Institute of Technology.

## Visitors to U. S.

**J. A. Böök,** heredity researcher at the University of Lund, Sweden, will be engaged in social-medical studies at the University of Minnesota this year.

Recent visitors at the National Bureau of Standards were **P. Grivet,** professor of physics at Ecole Normale Supérieure, Sorbonne, Paris; **L. Shahed** and **Y. E. Wakil,** army dentists to the Egyptian Army Medical Corps; **John Rogers,** resident lecturer with the School of Mines and Metallurgy, University of Otago, Dunedin, New Zealand.

## Grants and Awards

A three-year research fellowship of $2500 a year, established at the Purdue University School of Pharmacy by **Smith, Kline and French Laboratories of Philadelphia,** has been awarded to Charles F. Peterson. Mr. Peterson is working toward his Ph.D. degree in pharmacy, on "A Study of the Rectal Administration of Medicinal Substances."

The fourth annual award of the **Mary Soper Pope Medal** for distinguished accomplishment in botanical science, given by the Cranbrook Institute of Science, was presented at the AAAS annual meeting to a Carnegie Institution of Washington research team. The team, which is working at the Stanford laboratory in California, is headed by Jens Clausen, geneticist; the other two recipients are David D. Keck, taxonomist, and William M. Hiesey, physiologist. The principal joint investigations of the three men, who have worked together over a period of two decades, are in the field of experimental taxonomy, combining the concepts and tools of genetics, cytology, ecology, and geography.

The Pope medal was given last year to William Vogt for his work in conservation, especially in Latin America. Previously the medal had been awarded to C. C. Deam, Indiana state botanist, and to Frans Verdoorn, publisher of Chronica Botanica, for his work in improving international relations in plant sciences.

The **Adolphe Wetrems Prize** in physics and mathematics has been awarded by the Belgian Royal Academy of Sciences, Letters and Fine Arts to René Bailly, assistant professor in the Department of Geology, Washington University, St. Louis. This prize of $3000 is awarded every two years for work of value in science.

T. A. Boyd, of General Motors Research Laboratories, was presented the **Horning Memorial Award** by the Society of Automotive Engineers

on January 11, at the society's annual meeting at Detroit. The award honors Mr. Boyd's outstanding contributions during his 30-year study of fuels and engines.

## Fellowships

**Six Daniel and Florence Guggenheim Jet Propulsion Fellowships** of $2,000 a year each will be awarded this year. Granted for a period of two years, they are open to qualified applicants for advanced study in the fields of rocket and jet propulsion engineering. Three of the postgraduate fellowships are for work at Princeton University and the other three at the California Institute of Technology at the Jet Propulsion Centers established at the two institutions in 1948 by the Guggenheim Foundation.

**The 1950–51 Tau Beta Pi fellowships** are available to members doing graduate work in engineering. Each $1,200 fellowship is payable in ten monthly installments, and at least seven awards will be made. Application blanks and information can be obtained from Paul H. Robbins, Director of Fellowships, 1121 15th Street, N.W., Washington 5, D. C. Applications must be mailed by *February 28*. Awards will probably be announced by March 31.

**The establishment of a foundation for encouraging microbiological investigations in France,** to be known as the Waksman Foundation, has been approved by the trustees of Rutgers University Research and Endowment Foundation, which holds the patents on streptomycin and other antibiotics developed by Selman A. Waksman of the university's Department of Microbiology. The foundation was launched with an initial contribution of three million francs from Rhone-Poulenc, French chemical concern which has recently been licensed by the Rutgers Research and Endowment Foundation to engage in the manufacture of streptomycin in France. Royalties due the Rutgers Foundation from this company and any other French licensees will be paid to the French foundation. The funds will be used to support research on antibiotics and other problems in the field of microbiology in France.

Four grants, totaling 2,140,000 francs, were proposed by the Committee of the French Foundation at its first meeting last month. Three of the grants will go to workers at the Pasteur Institute in collaboration with various hospitals in Paris, the other to a staff member of the Biochemical Laboratories of the Ministry of the Colonies. Members of the foundation's executive committee are S. M. Delepine, of the French Institute and the French Academy of Medicine; Jacques Trefouel, member of the French Institute and director of the Pasteur Institute; and R. Paul, scientific director of Rhone-Poulenc.

**The Department of Physics of the University of Texas** is accepting applications for graduate teaching fellowships for the year 1950–51. These fellowships are open to students with a master's degree or its equivalent who are candidates for the doctorate. They are for a period of nine months and pay $1,620 for three-fourths time and $1,080 for half-time teaching. Nonresident students who become appointees may apply to the Dean of the Graduate School for a nonresident tuition scholarship which would remit a large part of the nonresident tuition. Applications stating qualifications and personal data, and including letters of recommendation, should be sent to the chairman of the department. Appointments will be made April 1, 1950.

## Colleges and Universities

An intensive search for antivirotics —substances of microbial origin which may prove effective against viruses—has been inaugurated by the **Rutgers University Department of Microbiology.** The new laboratory, to be known as the Virus Research Laboratory, will be headed by Vincent Groupé, associate professor of microbiology, and staffed by a chemist, a bacteriologist, and a group of graduate students and assistants. The building, which is the first unit of the university's planned Institute of Microbiology, is located on the grounds of the New Jersey Agricultural Experiment Station and was financed by a grant from the Rutgers Research and Endowment Foundation. The virus investigations were made possible by a grant of $25,000 from the Kresge Foundation of Detroit.

A course in clinical neurology will be presented at the **University of Minnesota Center for Continuation Study** from January 30 to February 11. The course has been planned particularly for neurologists, psychiatrists, pediatricians, internists, and neurosurgeons. Visiting faculty members include Fred Mettler, Neurological Institute, Columbia University; Walter Klingman, Department of Neurology, University of Virginia Hospital; Harold Voris, Neurological Surgery, Mercy Hospital, Chicago; Earl Walker, Neurological Surgery, Johns Hopkins University.

## Meetings and Elections

**The Injection Molding of Polystyrene** will be the subject of a symposium to be held by the Institute of Polymer Research at the Polytechnic Institute of Brooklyn January 28, with Turner Alfrey, Jr. as chairman.

**A seminar on the status of fundamental research in the psychophysiology of vision** will be held at Columbia University, January 30–31, under the sponsorship of the Office of Naval Research and directed by Henry A. Imus, head of the Psychophysiology Branch. Clarence H. Graham, professor of psychology at Columbia University and a member of the ONR Advisory Panel for Psychophysiology, will lead the discussion. Lyle Lanier, of New York University, will represent the Panel on Human Engineering and Psychophysiology of the Research and Development Board. Donald G. Marquis, executive secretary, will represent the Armed Forces-NRC Vision Committee.

**The American Chemical Society** will open its 117th national meeting in Houston, Texas, on March 26. The Houston session will continue until March 30; the second session

will be held in Philadelphia April 9–13; and the third in Detroit April 16–20. More than ten thousand American chemists and chemical engineers are expected to attend the three sessions. "Chemicals from Petroleum" will be the theme of one of the principal symposia at the Houston meeting. The role of vitamin $B_{12}$ in animal and human nutrition, new insight into the molecular structure of matter, and recent discoveries in the physical chemistry of bone are among other subjects to be discussed in several hundred papers during technical session held under the sponsorship of 18 professional divisions of the society.

**A conference on the teaching of the earth sciences in secondary schools** will be held at Boston University March 17–18. C. W. Wolfe, chairman of the Geology Department at Boston University, is chairman of the conference, which is being sponsored by the Earth Science Institute. Information and material may be had by writing to the Executive Secretary, The Earth Science Institute, Revere, Massachusetts.

L. M. Graves, of the University of Chicago, was elected first vice president of the **Mathematical Association of America** at its annual meeting held at Columbia University on December 30. He succeeds Saunders MacLane, also of the University of Chicago. Continuing in office are R. E. Langer, University of Wisconsin, president; N. H. McCoy, Smith College, second vice president; and H. M. Gehman, University of Buffalo, secretary-treasurer. M. R. Hestenes, of the University of California at Los Angeles, and Marie J. Weiss, of Sophie Newcomb College, were elected members of the board of governors for a two-year term.

## NRC News

A report entitled ***Foreign Research Opportunities for Graduate Students in Geography*** has been prepared by the Committee on Opportunities for Foreign Geographic Research, Earl B. Shaw, chairman.

The first part of the report contains an explanation of the efforts to gather information on the subject, and general suggestions on the best procedure to be followed in presenting a geographical research problem to an organization which might be interested in supporting it. It is suggested that the aspects of business and industry to which geography can contribute are primarily the selection of an industrial location, and the locating of marketing opportunities. Some of the problems to be considered in each of these fields are listed, and the responsibility of the professional geographer to industry and to his science is stressed. The second part of the report lists possible sources for support of foreign geographical research, including business organizations which may aid the research if it is related to the firm's own problems; colleges, universities, foundations, and scientific societies; and interested government organizations.

The report is available without charge from the Division of Geology and Geography, National Research Council, 2101 Constitution Avenue, Washington 25, D. C.

**The American Meteorological Society** is a new affiliate of the NRC in the Division of Mathematical and Physical Sciences. The society has nominated Carl-Gustaf Rossby, professor of meteorology, University of Chicago, and past president of the society, as its first NRC representative. Dr. Rossby is known for his theoretical work in general fluid circulation, both in the atmosphere and in the ocean.

**Five reports of the Nuclear Science Series** are available from the NRC without charge, on request from active workers in nuclear science: Nuclear Electric Quadrupole Moments and Quadrupole Couplings in Molecules, by B. T. Feld; Energy Levels of Light Nuclei, by Thomas Lauritsen; Neutrons from Alpha Emitters, by H. L. Anderson; Monoenergetic Neutrons from Charged Particle Reactions, by A. O. Hansen and R. F. Taschek; and Photoneutron Sources, by Albert Wattenberg.

A composite report is now available on the five regional conferences on **University Research and Patent Problems,** which the NRC Patent Policy Survey held in Denver, Berkeley, Chicago, New York, and Atlanta last spring. The report contains summary digests of the proceedings of each of the conferences and a composite resumé of the research and patent problems discussed. It is organized in chapters dealing with these problems under the following topical groupings: need for a university patent policy, unorganized research, organized research, sponsored research, patent management, and principles and considerations involved in formulating research and patent policies. The paper on research, inventions, and patents, delivered at the Denver conference by George N. Robillard, assistant chief of Naval Research (for patents) is also included. The report may be obtained for $1.00 per copy from the Patent Policy Survey, National Research Council, 2101 Constitution Avenue, Washington 25, D. C.

## Deaths

**Hermann Nilsson-Ehle,** professor emeritus of genetics at the University of Lund, Sweden, died in Lund on December 29 at the age of 77. He was known for his research in genetics and plant breeding and had been a member of the International Commission for Genetics Congresses since 1911.

**Marcos Tubangui,** head of the Department of Parasitology, Institute of Hygiene, Philippines, and professor of helminthology, died October 26. Dr. Tubangui was authority on the epidemiology, life cycle, treatment, and control of parasitic worms.

**Sam Rosenfeld, Jr.,** 41, associate professor of therapeutics at Ohio State University, died December 7 of coronary thrombosis. Dr. Rosenfeld had also served as senior clinician at the Columbus cancer clinic for the past three years.

**Isaiah Bowman,** president emeritus of Johns Hopkins University, died of a heart attack on December 26 at the age of 71. One of the world's foremost geographers, Dr. Bowman had in recent months served as chairman of the European Co-

operation Administration's committee on overseas territories. He was also writing a book at the time of his death.

**J. Francis Smith,** professor emeritus of neurology and psychiatry at the Philadelphia College of Osteopathy, died at his home in Philadelphia at the age of 53. Dr. Smith had served on the staff of the college for 17 years before his retirement in world war, serving in France with 1945. He was blinded in the first the Royal Canadian Army.

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**The Federation of American Scientists** has recently been reorganized as a national society with chapters in ten scientific centers throughout the country. The federation is active in matters where science touches on public affairs, particularly the control of atomic energy, and sponsors meetings comparable to technical sessions of scientific societies. The reorganization makes it possible for scientists in all parts of the country to take a more active part in the work of the federation. National headquarters of the federation are located at 1749 L Street, N.W., Washington 6, D. C.

**A new geography of world petroleum** has been completed by a group of petroleum geologists under the sponsorship of the American Geographical Society. The volume, titled *World geography of petroleum*, will be published early this year by Princeton University Press. The work was done under the editorship of the geologist Wallace Pratt, with the assistance of Dorothy Good, of the American Geographical Society, and will contain much new material, including fifty specially prepared maps and numerous tables and diagrams.

**A series of one-week teacher training courses in the medical hazards of atomic warfare** is being sponsored by the U. S. Atomic Energy Commission, in cooperation with the National Security Resources Board and the General Services Administration. The courses will provide information and materials to selected members of the medical profession, who in turn will instruct physicians, dentists, and nurses in local areas as part of state and municipal civil defense programs.

The first of the courses will be held in March at the Argonne National Laboratory, the University of Rochester, and Western Reserve University School of Medicine. Courses will be offered later in the spring at the University of California at Los Angeles, the University of Utah School of Medicine, University of Alabama School of Medicine, and Johns Hopkins School of Medicine.

**The Wellcome Historical Medical Library** in London was formally opened last month. This library of more than 200,000 volumes has been built up over the past fifty years, and represents a private interest of the late Sir Henry Wellcome. The collection of books printed before 1500 A.D. contains 632 volumes and the 16th century collection of 4,000 volumes is equally important. Special collections include works on travel, botany, alchemy, occultism, tobacco, plague, archaeology, anthropology, and folklore. There is also a large modern selection. Although the library is for reference only and no books can be lent there are ample accommodations for readers, including microfilm and photostatic service. Historical and bibliographical inquiries, which should be made by letter, will be answered by the library staff. Scientific societies and other such groups can arrange for special visits to the library. A general catalogue is being prepared.

***Fertility and Sterility,*** the new journal of the American Society for the Study of Sterility, will appear for the first time this month. It will contain original articles derived from the fundamental, medical, or veterinary sciences relating to the diagnosis and treatment of human infertility. Pendleton Tompkins is the editor.

## Recently Received—

***Public Health Research Institute of the City of New York: Annual Report 1948–49. City of New York, Inc.*** Foot of East 15th Street, New York City.

***Synopsis of Researches at the Bengal Immunity Laboratory, May 1947–April 1948.*** Bengal Immunity Research Institute, 39, Lower Circular Road, Calcutta 16, India.

***Effects of Feeding DDT-Sprayed Insects to Fresh-Water Fish.*** Special Scientific Report, Fisheries No. 3. Fish and Wildlife Service, U. S. Department of Interior, Washington, D. C.

***Selected Bibliography of the Specialized Agencies Related to the United Nations.*** Columbia University Press, Morningside Heights, New York City. 25 cents.

***Annual Reports of the Technical Committees, Institute of Navigation, May 1948–49.*** University of California, Los Angeles 24.

***Sugar Derivatives: A Survey of Potential Production Costs.*** Harold E. Bode. Technological Report Series, No. 6. Sugar Research Foundation, Inc., New York City.

***The Intensities of Isotopic Carbon Bands in the Spectra of Twenty-One R-Type Stars.*** Vol. 7, No. 26. Andrew McKellar. Department of Mines and Resources, Dominion Astrophysical Observatory, Victoria, B. C., Canada.

## Make Plans for—

**Southern Association of Science and Industry,** winter meeting, January 23–24, Hotel Roosevelt, New Orleans, Louisiana.

**Sixth Annual Conference on Protein Metabolism,** sponsored by the Bureau of Biological Research, Rutgers University, January 27–28, on the campus.

**Third annual symposium on modern methods of analytical chemistry,** sponsored by the College of Chemistry and Physics, Louisiana State University, January 30–February 2, on the campus.

**American Physical Society,** 297th meeting, February 2–4, Columbia University, New York City.

# Personnel Placement

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**Geology** related work desired by physical-inorganic chemist. M.S. 1939. State salary. Box 5, SCIENCE. X

**Infrared Spectroscopist:** Physical chemist, 50, civil service status, employed. Three years current experience Perkin-Elmer equipment. Desire continue infrared on research basis. Now grossing about $6500; need large percentage increase for taxes, inflation, television. Box 8, SCIENCE. X

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**Pharmacologist:** Senior position in laboratory of a pharmaceutical manufacturing firm with extensive screening and research program. Candidates should have M.D. degree. Metropolitan location, Eastern. Box 9, SCIENCE. X

**Physiologist–Pharmacologist:** M.S. or Ph.D. to instruct in physiology and pharmacology for second semester. May be permanent. Department of Pharmacology, College of Pharmacy, University of Florida, Gainesville, Florida. 1/27

Positions Open:
(a) **Assistant medical director**; pharmaceutical industry; duties combination of clinical research and plant health supervising; Middle West. (b) **Biochemist** with agricultural experiment station experience or training; food industry; East. (c) **Parasitologist**, Ph.D. in parasitology with minor in bacteriology; medical school department of medicine; duties: teaching and research; Middle West. (d) **Chemist** to work on isolation of active agent present in serum albumin and, also, research worker to perform experiments in research on aging; Master's degrees required; research division, university medical school; East. (e) **Physician** with scientific background to serve in research capacity in radioisotope unit, large teaching hospital. (f) **Pharmacologist**; preferably Ph.D. with broad knowledge of physiological activity and pharmacology of important drugs; laboratory experience and supervisory ability desirable. S1-3 Burneice Larson, Medical Bureau, Palmolive Building, Chicago. X

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